STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 94798

TO: David Lukton **Location:** **Art Unit: 1653** **May 29, 2003** **Case Serial Number: 581511**	**From: P. Sheppard** **Location: CM1-1E03** **Phone: (703) 308-4499** **sheppard@uspto.gov**

Search Notes

2

Access DB# 94498

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: David Lukton Examiner #: 71263 Date: 05-22-03
Art Unit: 1653 Phone Number 308-3213 Serial Number: 09-581511
Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL
MailBox: 9B01 ; Exr Rm: 9B05
If more than one search is submitted, please prioritize searches in order of need.
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Title of Invention: HEMIASTERLIN ANALOGS

Applicants: ANDERSEN, RAYMOND; PIERS, EDWARD; NIEMAN, JAMES; COLEMAN, JOHN; ROBERGE, MICHEL

Earliest Priority Date: 12/19/97

* * * * * *

Applicants are claiming the compounds below

R1, R2, R4 = anything

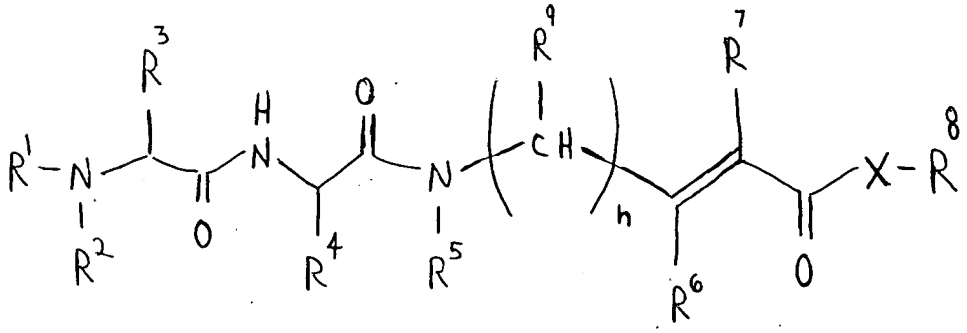
R6, R7, R8, R9 = anything

R3 is anything other than the side chain of tryptophan (i.e., indole-methylene)

R5 is anything other than hydrogen

X = -O- or -NH-

n = an integer of 0 - 2.



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STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
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Searcher Phone #: _____	AA Sequence (#)_____		Dialog _____	
Searcher Location: _____	Structure (#)	_____	Questel/Orbit _____	
Date Searcher Picked Up: _____	Bibliographic	_____	Dr.Link _____	
Date Completed: 5/29/03	Litigation	_____	Lexis/Nexis_____	
Searcher Prep & Review Time: _____	Fulltext	_____	Sequence Systems _____	
Clerical Prep Time: _____	Patent Family	_____	WWW/Internet _____	
Online Time: _____	Other	_____	Other (specify)_____	

PTO-1590 (8-01)

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 14:30:55 ON 29 MAY 2003
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FILE COVERS 1907 - 29 May 2003  VOL 138 ISS 22
FILE LAST UPDATED: 28 May 2003  (20030528/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

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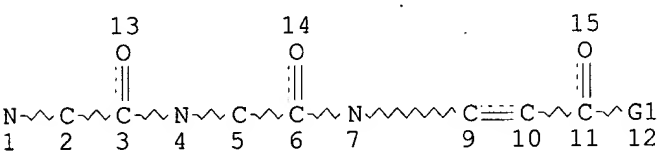


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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
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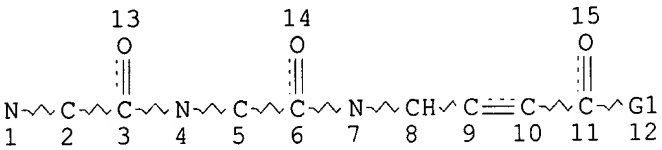


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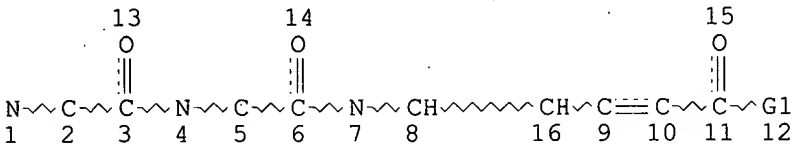
R 2052 OR 2051
L5 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
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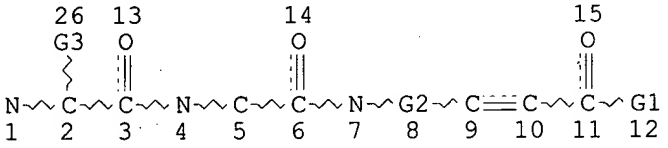

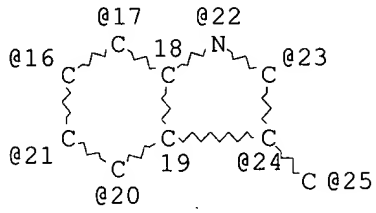

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
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L14 54 SEA FILE=HCAPLUS ABB=ON PLU=ON L13
L15 31 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND PD<DECEMBER 19, 1997

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=> d ibib abs hitrn l15

L15 ANSWER 1 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:650062 HCAPLUS
DOCUMENT NUMBER: 129:290436
TITLE: Pseudo- and non-peptide bradykinin receptor antagonists
INVENTOR(S): Kyle, Donald James; Mavunkel, Babu Joseph;

Chakravarty, Sarjavit; Lu, Zhijian
PATENT ASSIGNEE(S): Scios Inc., USA
SOURCE: U.S., 40 pp., Cont.-in-part of U.S. Ser. No. 353,426, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 5817756	A	19981006	US 1995-401595	19950309	
US 5444048	A	19950822	US 1993-118981	19930909	<--
US 5552383	A	19960903	US 1993-118550	19930909	<--
US 5541286	A	19960730	US 1994-281907	19940728	<--
US 5686565	A	19971111	US 1994-281904	19940728	<--
US 5610142	A	19970311	US 1995-416524	19950403	<--

PRIORITY APPLN. INFO.:
US 1993-118550 A2 19930909
US 1993-118558 B2 19930909
US 1993-118981 A2 19930909
US 1993-119341 B2 19930909
US 1994-281904 A2 19940728
US 1994-281906 B2 19940728
US 1994-281907 A2 19940728
US 1994-281908 B2 19940728
US 1994-353426 B2 19941209
US 1992-957879 A2 19921008

OTHER SOURCE(S): MARPAT 129:290436
AB Pseudopeptides X-Y-Z (X = arginine or lysine residue, Y is a hydrophobic org. moiety having a nitrogen atom at the X-Y junction and a carbonyl group at the Y-Z junction, Z is an arrangement of atoms which inherently adopts a beta turn conformation and has a pos. charge near the distal end) were prepd. as bradykinin receptor antagonists. Thus, H-D-Arg-Arg-NH-p-C6H4N(COPh)CH2CONHCH2-o-C6H4CH:CHCH:CHCO-Arg-OH was prepd. and showed Ki = 36 nM for binding of the human B2 bradykinin receptor.
IT **168824-56-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pseudo- and non-peptide bradykinin receptor antagonists)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitrn l15 2-31

L15 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:757024 HCAPLUS
DOCUMENT NUMBER: 128:13442
TITLE: Preparation of alkene pseudopeptides as picornavirus 3C protease inhibitors
INVENTOR(S): Webber, Stephen E.; Dragovich, Peter S.; Prins, Thomas J.; Reich, Siegfried H.; Little, Thomas L., Jr.; Littlefield, Ethel S.; Marakovits, Joseph T.; Babine, Robert E.; Bleckman, Ted M.
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9743305	A1	19971120	WO 1997-US8112	19970513	<--
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RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
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CA 2254343	AA	19971120	CA 1997-2254343	19970513	<--
AU 9730059	A1	19971205	AU 1997-30059	19970513	<--
AU 722704	B2	20000810			
ZA 9704108	A	19980820	ZA 1997-4108	19970513	
EP 910572	A1	19990428	EP 1997-924707	19970513	
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JP 2000506903	T2	20000606	JP 1997-541076	19970513	
KR 2000011019	A	20000225	KR 1998-709169	19981113	
US 6214799	B1	20010410	US 1999-226205	19990107	
US 6362166	B1	20020326	US 2000-689717	20001013	

PRIORITY APPLN. INFO.:	US 1996-17666P	P	19960514
	US 1996-645687	A	19960514
	US 1997-850398	A	19970502
	WO 1997-US8112	W	19970513
	US 1999-226205	A3	19990107

OTHER SOURCE(S): MARPAT 128:13442

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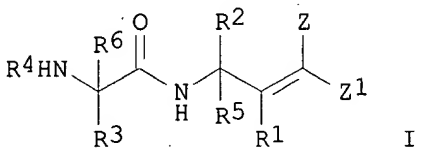

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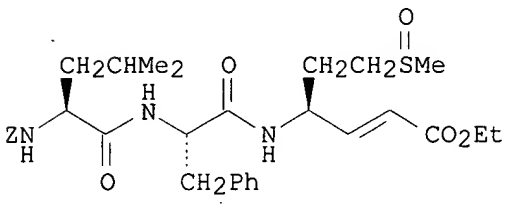

II

AB Picornaviral 3C protease inhibitors I [R1 = H, F, alkyl, OH, SH, O-alkyl, S-alkyl; R2, R5 = independently H, XY1A1(B1)D1, alkyl group different from XY1A1(B1)D1, with the proviso that both R2 and R5 .noteq. H and when R2 or R5 = XY1A1(B1)D1, X = CH or CF and Y1 = CH or CF;R3, R6 = independently H, F, alkyl; ZR4 = H, OH, suitable org. group; Z, Z1 = independently H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, etc; XY1 form 3-membered ring with Q1, Q1 = CR10R11, O, X = CH, CF, Y = CH, CF, C-alkyl; R10, R11 = independently H, halo, alkyl; CR10R11 = cycloalkyl,

heterocycloalkyl; X = CH2, CF2, CHF, S; Y1 = O, S, NR12,, CR12R14, CO, CS, C(CR13R14); R12 = H, alkyl; R13, R14 = independently H, F, alkyl; CR13R14 = cycloalkyl, heterocycloalkyl; A1 = C, CH, CF, S, P, Se, N, NR15, S(O), Se(O), P(OR15), P(NR15R16); R15, R16 = independently alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl; D1 = moiety contg. electron lone pair capable of forming hydrogen bond; B1 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, OR17, SR17, NR1718, NR19NR17R18, NR17OR18; R17-R19 = H, any group R15; with provisos], and pharmaceutically acceptable salts thereof and prodrugs thereof, obtainable by chem. synthesis, inhibit or block the biol. activity of picornaviral 3C proteases. These compds., as well as pharmaceutical compns. that contain these compds., are suitable for treating patients or hosts infected with one or more picornaviruses. Several novel methods and intermediates can be used to prep. the novel picornaviral 3C protease inhibitors of the present invention. Thus, olefination of protected peptide aldehyde Z-L-Leu-L-Phe-L-Met(O)-H (Z = PhCH2O2C), prepd. in 3 steps from L-methioninol and Z-L-Leu-L-Phe-OH, with (carbethoxymethylene)triphenylphosphorane gave 74% title compd. II. II and related alkene pseudopeptides were tested for inhibition of rhinovirus protease, with II showing Ki = 4.3 .mu.M.

IT **199003-72-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of alkene pseudopeptides as picornavirus 3C protease inhibitors)

IT **199003-71-9P 199003-73-1P 199003-74-2P 199003-75-3P 199003-76-4P 199003-77-5P 199003-78-6P 199003-81-1P 199003-82-2P 199003-85-5P 199003-86-6P 199003-87-7P 199003-88-8P 199003-89-9P 199003-92-4P 199003-95-7P 199004-05-2P 199004-06-3P 199004-07-4P 199004-10-9P 199004-19-8P 199004-20-1P 199004-21-2P 199004-22-3P 199004-27-8P 199004-28-9P 199004-29-0P 199004-30-3P 199004-31-4P 199004-55-2P 199004-56-3P 199004-57-4P 199004-58-5P 199004-59-6P 199004-60-9P 199004-61-0P 199004-62-1P 199004-63-2P 199004-64-3P 199004-66-5P 199004-68-7P 199004-69-8P 199004-70-1P 199004-71-2P 199004-72-3P 199004-73-4P 199004-74-5P 199004-75-6P 199004-76-7P 199004-77-8P 199004-78-9P 199004-79-0P 199004-80-3P 199004-89-2P 199004-90-5P 199004-91-6P 199004-92-7P 199004-93-8P 199004-94-9P 199004-95-0P 199004-96-1P 199004-97-2P 199004-98-3P 199004-99-4P 199005-00-0P 199005-01-1P 199005-03-3P 199005-05-5P 199005-06-6P 199005-07-7P 199005-09-9P 199005-10-2P 199005-11-3P 199005-12-4P 199005-13-5P 199005-14-6P 199005-15-7P 199005-16-8P 199005-17-9P 199005-19-1P 199005-20-4P 199005-21-5P 199005-23-7P 199005-24-8P 199005-25-9P 199005-26-0P 199005-28-2P 199005-29-3P 199005-30-6P 199005-31-7P 199005-32-8P 199005-33-9P 199005-34-0P 199005-35-1P 199005-36-2P 199005-37-3P 199005-38-4P 199005-40-8P 199005-41-9P 199005-42-0P 199005-43-1P 199005-44-2P 199005-46-4P 199005-48-6P 199006-67-2P 199007-58-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of alkene pseudopeptides as picornavirus 3C protease inhibitors)

IT **199005-60-2P 199005-72-6P 199005-73-7P**
199005-76-0P 199005-78-2P 199005-80-6P
199005-84-0P 199006-12-7P 199006-18-3P
199006-20-7P 199006-40-1P 199006-41-2P
199006-47-8P 199006-48-9P 199006-53-6P
199006-60-5P 199006-61-6P 199006-64-9P
199006-65-0P 199006-66-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of alkene pseudopeptides as picornavirus 3C protease inhibitors)

L15 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:746070 HCAPLUS
DOCUMENT NUMBER: 128:30375
TITLE: Auto-deconvoluting combinatorial libraries of compounds interacting with enzymes, receptors, or other active moieties
INVENTOR(S): Quibell, Martin; Johnson, Tony; Hart, Terance
PATENT ASSIGNEE(S): Peptide Therapeutics Limited, UK; Quibell, Martin; Johnson, Tony; Hart, Terance
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9742216	A1	19971113	WO 1997-GB1158	19970424 <--
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RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2252408	AA	19971113	CA 1997-2252408	19970424 <--
AU 9726450	A1	19971126	AU 1997-26450	19970424 <--
AU 728263	B2	20010104		
EP 906334	A1	19990407	EP 1997-918253	19970424
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JP 2000512979	T2	20001003	JP 1997-539622	19970424
ES 2162277	T3	20011216	ES 1997-918252	19970424
US 2003092067	A1	20030515	US 2002-259420	20020930

PRIORITY APPLN. INFO.:

GB 1996-8457	A	19960424
GB 1996-16115	A	19960731
GB 1996-24584	A	19961127
WO 1997-GB1158	W	19970424
US 1999-171680	A3	19991103

AB The present invention relates to the field of app. (set of compds.) and methods which provide the rapid generation of structure/activity relationships using auto-deconvoluting combinatorial libraries, which facilitate the invention of novel active compds. The invention provides app. and methods which can be used for the rapid generation of

structure/activity relationship (SAR) data, and, therefore, the characterization of the active motif of any group of compds. The invention provides libraries of compds. which interact with an active moiety, and app. and methods to identify such compds. The active moieties may be (but are not limited to) enzymes (e.g. kinases), receptors, antibodies, etc. The interaction of the active moiety with the compds. of the library may be (but is not limited to) the interaction of a substrate or inhibitor with an enzyme, the interaction of a ligand with a receptor, the interaction of an antigen or antigenic epitope with an antibody, etc. The invention describes e.g. the synthesis of a no. of compds. for use as a library for screening for potential substrates for dust mite Der P1 cysteine protease, as well as subsequent identification and synthesis of active inhibitors of the enzyme.

IT **187991-61-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(auto-deconvoluting combinatorial libraries of compds. interacting with enzymes, receptors, or other active moieties)

L15 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:717935 HCAPLUS
DOCUMENT NUMBER: 128:1461
TITLE: Substrates and inhibitors of proteolytic enzymes
INVENTOR(S): Quibell, Martin; Johnson, Tony; Hart, Terance
PATENT ASSIGNEE(S): Peptide Therapeutics Ltd., UK; Quibell, Martin; Johnson, Tony; Hart, Terance
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9740065	A2	19971030	WO 1997-GB1157	19970424	<--
WO 9740065	A3	19971204			
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RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9726449	A1	19971112	AU 1997-26449	19970424	<--
AU 706855	B2	19990624			
CA 2252408	AA	19971113	CA 1997-2252408	19970424	<--
EP 906333	A2	19990407	EP 1997-918252	19970424	
EP 906333	B1	20010725			
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JP 2001501170	T2	20010130	JP 1997-537864	19970424	
AT 203545	E	20010815	AT 1997-918252	19970424	
ES 2162277	T3	20011216	ES 1997-918252	19970424	
US 6528275	B1	20030304	US 1999-171680	19991103	
US 2003092067	A1	20030515	US 2002-259420	20020930	

PRIORITY APPLN. INFO.:
GB 1996-8457 A 19960424
GB 1996-16115 A 19960731
GB 1996-24584 A 19961127
WO 1997-GB1157 W 19970424
US 1999-171680 A3 19991103

AB The present invention relates to the field of compds. which are substrates or inhibitors of proteolytic enzymes and to app. and methods for identifying substrates or inhibitors for proteolytic enzymes. We have devised a combinatorial method for the rapid identification of binding motifs which will greatly expedite the synthesis of inhibitors of a variety of proteolytic enzymes such as aspartyl proteases, serine proteases, metallo proteases and cysteinyl proteases. Some inhibitors have the formula A-B-C-D-nE-F, in which A represents a fluorescor internally quenched by F; while B, C, D, and E represent groups such that the scissile bond between any two of these groups is a suitable bond; n is an integer 1, 2, 3, or 4; and F a quencher capable of internally quenching the fluorescor A.

IT **187991-61-3P 187991-62-4P 187991-63-5P**
187991-64-6P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(substrates and inhibitors of proteolytic enzymes)

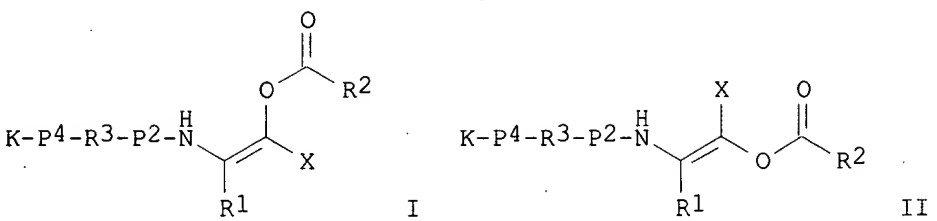
L15 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:491631 HCAPLUS
DOCUMENT NUMBER: 127:95620
TITLE: Preparation of acylated enol derivatives of .alpha.-ketoesters and .alpha.-ketoamides as neutrophil-associated inflammation inhibitors
INVENTOR(S): Peet, Norton P.; Burkhart, Joseph P.; Mehdi, Shujaath
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9720856	A1	19970612	WO 1996-US17752	19961104	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2239159	AA	19970612	CA 1996-2239159	19961104	<--
CA 2239159	C	20020910			
AU 9676697	A1	19970627	AU 1996-76697	19961104	<--
AU 705819	B2	19990603			
EP 863915	A1	19980916	EP 1996-939555	19961104	
EP 863915	B1	20000202			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CN 1203602	A	19981230	CN 1996-198733	19961104	
AT 189457	E	20000215	AT 1996-939555	19961104	
JP 2000502073	T2	20000222	JP 1997-521265	19961104	
ES 2144788	T3	20000616	ES 1996-939555	19961104	
ZA 9609889	A	19970617	ZA 1996-9889	19961125	<--
TW 419482	B	20010121	TW 1996-85114600	19961126	
NO 9802467	A	19980803	NO 1998-2467	19980529	

PRIORITY APPLN. INFO.: US 1995-566196 A 19951201
WO 1996-US17752 W 19961104

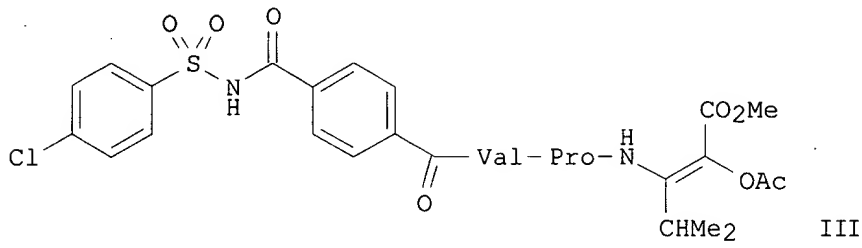
OTHER SOURCE(S): MARPAT 127:95620

GI



I

II



III

AB This invention relates to title compds. I and II [R1 = C1-4 alkyl; R2 = C1-4 alkyl, Ph, CH2Ph, cyclohexyl, cyclohexylmethyl; X = CO2R2, CONHR3, R3 = H, any group in R2; P2 = Gly, Ala where N.alpha. is optionally substituted with C1-6 alkyl, optionally fused C3-12 cycloalkyl, C3-12 cycloalkyl-C1-6 alkyl, C4-11 bicycloalkyl, C4-11 bicycloalkyl-C1-6 alkyl, C6-10 aryl, C6-10 aryl-C1-6 alkyl, C3-7 heterocycloalkyl, C3-7 heterocycloalkyl-C1-6 alkyl, C5-9 heteroaryl, C5-9 heteroaryl-C1-6 alkyl, Pro, 2-azetidinecarbonyl, 2-indolylcarbonyl, 1,2,3,4-tetrahydroisoquinoline-3-carbonyl, pipecolyl, thiazolidine-4-carbonyl; Hyp(CH2Ph), Hyp(Ac), Hyp; P3 = Ala, .beta.-Ala-, Leu, Ile, Nle, Val, Nva, Lys, .beta.-Val; P4 = Ala, .beta.-Ala, Val, Nva, .beta.-Val, Pro, bond; K = H, Ac, succinyl, Bz, Me3CO2C (Boc), phCH2O2C (Cbz), dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulfonyl, 2-HO2CC6H4CO, CONMe2, 4-(4-ClC6H4SO2NHCO)C6H4CO, 4-(4-BrC6H4SO2NHCO)C6H4CO, 4-(H2NSO2C6H4SO2NHCO)C6H4CO, 3-(3-pyridyl)propionyl, R-B; R = 4-morpholinyl, 2-furyl; B = CO, CHR'CO, SO2, COCHR'CO, p-COC6H4CO, p-SO2C6H4CO, 2,5-pyridinedicarbonyl, p-CONHC6H4CO, (CH2)nNR'CO; R' = H, C1-4 alkyl; n = 0-2]. Compds. I and II are either prodrugs of known elastase inhibitors or are elastase inhibitors in their own right and are useful in the treatment of various inflammatory diseases, including cystic fibrosis and emphysema. Thus, acylation of 135 mg 4-(4-ClC6H4SO2NHCO)C6H4CO-Val-Pro-Val-CO2Me with 0.19 mL Ac2O in 1.0 mL pyridine gave 23 mg. acetyloxy ester III (MDL 105,565). III inhibited human neutrophil elastase at 99% at a concn. of 10 nM in an in vitro assay.

IT **192193-33-2P 192193-34-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ketoester and ketoamide acylated enol derivs. as neutrophil-assocd. inflammation inhibitors)

L15 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:220603 HCAPLUS
DOCUMENT NUMBER: 126:212446
TITLE: Tripeptide methyl ketone cysteine protease inhibitors for use in treatment of Ige mediated allergic diseases
INVENTOR(S): Johnson, Tony; Hart, Terrance; Laing, Peter; Shakib,

Farouk; Quibell, Martin
PATENT ASSIGNEE(S): Peptide Therapeutics Limited, UK; Johnson, Tony; Hart, Terrance; Laing, Peter; Shakib, Farouk; Quibell, Martin
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9704004	A1	19970206	WO 1996-GB1707	19960717	<--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM					
AU 9665242	A1	19970218	AU 1996-65242	19960717	<--
AU 716716	B2	20000302			
EP 839155	A1	19980506	EP 1996-924976	19960717	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 11509543	T2	19990824	JP 1996-506421	19960717	
US 6034066	A	20000307	US 1998-45	19980226	

PRIORITY APPLN. INFO.:
GB 1995-14616 19950717
GB 1995-22221 19951031
WO 1996-GB1707 19960717

OTHER SOURCE(S): MARPAT 126:212446

AB Tripeptide compds. were prepd for use in the treatment of allergic diseases, including juvenile asthma and eczema, via inhibition of the cysteine protease activity of Dermatophagoides pteronyssinus (Der p I), a major allergen of house dust mite. Compds. claimed included R1-CONH-XR2-CONH-YR3-CONH-ZR4-W [X, Y, Z = N, CH; R1 = nitrogen blocking group; R2, R3, R4 = side-chains on X, Y, Z; W = group that reacts irreversibly with active cysteine thiol of Der p I; R1 = hydrophobic Ph, 2-naphthyl, 9-anthracyl, heteroaryl optionally connected to heteroatom to carbonyl group, etc.; XR2 = Ala, Leu, Nle, Val, etc; YR3 = Lys, Gln, Met(O), Ala; ZR4 = Ala, Leu, Nle, Val, Ile, etc.; W = E-CH2CHO, E-CH2CH:CH2, E-CH2CH:CHCHO, R-CO2NCHO, Y-CH:CH2; E = aryloxy, arylthio, heteroaryl, halo, R-SO3, R2P(O)O, RCO2; R = alkyl, aryl; Y = ester, sulfone, carboxylate, amide, etc. groups]. E64, L-trans-epoxysuccinyl-leucylamido(4-guanidino)butane, is excluded from the claimed compds. Thus, Bz-Val-Ala-Nle-OH underwent successive treatment with iso-Bu chloroformate/N-methylmorpholine, CH2N2, and HBr/HOAc to give Bz-Val-Ala-Nle-CH2Br which reacted with 2,6-Cl2C6H3CO2OH to give Bz-Val-Ala-Nle-CH2O2CC6H3Cl2-2,6 (I). In Der p I enzyme inhibiting assay, I had a Kobs/[I] of 6.8 x 107 M-1 s-1.

IT **187991-62-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate in prepn. of tripeptide Me ketones with allergen inhibiting activity)

IT **187991-61-3P 187991-63-5P 187991-64-6P 187991-65-7P 187991-66-8P 187991-67-9P 187991-68-0P 187991-72-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tripeptide Me ketones with allergen inhibiting activity)

IT **187991-69-1P 187991-70-4P 187991-71-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of tripeptide Me ketones with allergen inhibiting activity)

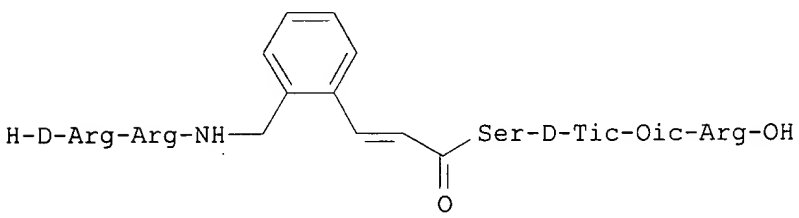
L15 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:494750 HCAPLUS
DOCUMENT NUMBER: 125:196389
TITLE: Bradykinin antagonist pseudopeptide derivatives of aminoalkenoic acids
INVENTOR(S): Kyle, Donald J.
PATENT ASSIGNEE(S): Scios Nova Inc., USA
SOURCE: U.S., 26 pp., Cont.-in-part of U.S. 5,444,046.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 5541286	A	19960730	US 1994-281907	19940728	<--
US 5521158	A	19960528	US 1992-957879	19921008	<--
US 5444048	A	19950822	US 1993-118981	19930909	<--
CA 2171446	AA	19950316	CA 1994-2171446	19940909	<--
WO 9507294	A1	19950316	WO 1994-US10128	19940909	<--
W: CA, JP, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 716661	A1	19960619	EP 1994-929158	19940909	<--
EP 716661	B1	20000405			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 11500100	T2	19990106	JP 1994-508795	19940909	
AT 191486	E	20000415	AT 1994-929158	19940909	
ES 2148347	T3	20001016	ES 1994-929158	19940909	
US 5817756	A	19981006	US 1995-401595	19950309	
US 5610142	A	19970311	US 1995-416524	19950403	<--

PRIORITY APPLN. INFO.:

US 1992-957879	A2	19921008
US 1993-118981	A2	19930909
US 1993-118550	A	19930909
US 1993-118558	A	19930909
US 1993-119341	A	19930909
US 1994-281904	A	19940728
US 1994-281906	A	19940728
US 1994-281907	A	19940728
US 1994-281908	A	19940728
US 1994-119341	A	19940909
WO 1994-US10128	W	19940909
US 1994-353426	B2	19941209

OTHER SOURCE(S): MARPAT 125:196389
GI



I

AB Pseudopeptide compds. A-B-C-D-E-F-G-Cn wherein: A is H or is selected from L- and D-isomers of, e.g., Arg, Gln, Asn, Lys; B is a bond or is selected from L- and D-isomers of Arg, Gln, Asn, Lys; C is a C2 to C18 olefinic aminoalkenoyl NH(CH2)mZ1(CH2)nZ2(CH2)oCO wherein Z1 and Z2 are independently selected from the group consisting of a bond, C3-8 carbocycle, C2-18 monoolefin or C4-18 polyolefin contg. 1-5 double bonds which may optionally be incorporated into a cyclic system; m, n, and o are independently 0-12, with the proviso that their total does not exceed 16; D is a bond or is selected from Ser, Thr, Gly, Val, Ala, Cys, and Tyr; E is selected from the group consisting of a D-arom. amino acid and a D-Hype (hydroxyproline ether/thioether); F is selected from, e.g., Oic, Aoc, Thz, Tic [Oic is (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid; Aoc is (S,S,S)-2-azabicyclo[3.3.0]octane-3-carboxylic acid; Thz is thiazolidine-4-carboxylic acid; Tic is tetrahydroisoquinoline-3-carboxylic acid]; G is selected from Arg, Orn, Asn, Gln, and Lys; Cn is OH or a C-terminal extension selected from, e.g., amide, alkoxy, based on a modified bradykinin sequence are potent bradykinin receptor antagonists. Amino acids at at positions 2 through 5 are replaced by olefinic aminoalkenoyl groups to reduce the peptide nature of the compds. The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites. Thus, e.g., pseudopeptide I was prepd. by solid-phase methodol., incorporating aminoalkenoyl spacer N-Boc-3-[2-(aminomethyl)phenyl]-2-propenoic acid (also prepd.); I exhibited binding to human bradykinin B2 receptor with K = 27 nM, and bradykinin antagonist activity with pA2 = 120 .+-. 8.

IT **168824-56-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bradykinin antagonist pseudopeptide derivs. of aminoalkenoic acids)

L15 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:108481 HCAPLUS
DOCUMENT NUMBER: 124:249227
TITLE: High-throughput purity estimation and characterization of synthetic peptides by electrospray mass spectrometry
AUTHOR(S): Smart, Swee S.; Mason, Tom J.; Bennell, Paul S.; Maeij, N. Joe; Geysen, H. Mario
CORPORATE SOURCE: Chiron Mimotopes Pty. Ltd., Victoria, Australia
SOURCE: International Journal of Peptide & Protein Research (**1996**), 47(1/2), 47-55
CODEN: IJPPC3; ISSN: 0367-8377
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English

AB High-throughput anal. for purity and mol. wt. detn. of synthetic peptides including characterization of any peptidic byproducts arising from synthesis is described. The data from electrospray mass spectrometry are processed with an algorithm that calcs. the contribution of the target peptide and each of the identifiable contaminants to the total ionizable material in a sample of synthetic peptide. All essential data were obtained by one instrumental technique in <3 min per sample. The technique has distinct advantages in the rapid anal. of the many hundreds of peptides/peptidomimetics required in systematic quant. structure-activity relation and other studies.

IT **175168-04-4**
RL: ANT (Analyte); ANST (Analytical study)
(detn. in synthetic peptides by electrospray mass spectrometry)

L15 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:846507 HCAPLUS

DOCUMENT NUMBER: 123:257408
TITLE: Preparation of peptide compounds as pseudo- and non-peptide bradykinin receptor antagonists
INVENTOR(S): Kyle, Donald James; Mavunkel, Babu Joseph; Lu, Zhijian
PATENT ASSIGNEE(S): Scios Nova Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9507294	A1	19950316	WO 1994-US10128	19940909	<--
W: CA, JP, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 5444048	A	19950822	US 1993-118981	19930909	<--
US 5552383	A	19960903	US 1993-118550	19930909	<--
US 5541286	A	19960730	US 1994-281907	19940728	<--
US 5686565	A	19971111	US 1994-281904	19940728	<--
EP 716661	A1	19960619	EP 1994-929158	19940909	<--
EP 716661	B1	20000405			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 11500100	T2	19990106	JP 1994-508795	19940909	
AT 191486	E	20000415	AT 1994-929158	19940909	
US 5610142	A	19970311	US 1995-416524	19950403	<--

PRIORITY APPLN. INFO.:

US 1993-118550	A	19930909
US 1993-118558	A	19930909
US 1993-118981	A	19930909
US 1993-119341	A	19930909
US 1994-281904	A	19940728
US 1994-281906	A	19940728
US 1994-281907	A	19940728
US 1994-281908	A2	19940728
US 1992-957879	A2	19921008
US 1994-119341	A	19940909
WO 1994-US10128	W	19940909

OTHER SOURCE(S): MARPAT 123:257408
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Peptide derivs. X-Y-Z [X = a moiety having a net pos. charge selected from a pos. charged amino acid and an org. group; Y = a hydrophobic org. moiety (e.g. Q - Q3) having the following characteristics: (a) a N junction at the X-Y junction, (b) a CO group at the Y-Z junction, (c) the hydrophobic org. moiety between the N atom and the CO group which is selected from a carbocyclic, a heterocyclic, and a linear org. moiety, (d) an at. group in the range of 135-300 .ANG., (e) an allowed conformation such that an end-to-end distance between the flanking N and CO atoms is .apprx.5.0.+-.1.5 .ANG., and (f) provided that Y cannot consist of naturally occurring amino acids; Z = an arrangement of atoms which inherently adopt a .beta.-turn conformation and has a pos. charge near the distal end] are prepd. ABS wherein many (or all) of the peptide bonds of bradykinin are eliminated to yield compds. having, in appropriate spatial arrangement, two pos. charged moieties flanking a hydrophobic org. moiety and a moiety which mimics a beta turn conformation, and having the ability to specifically compete with native bradykinin for binding to the bradykinin B2 receptor. A pharmaceutical prepn. for treating local pain

and inflammation form burns, wounds, cuts, rashes, or other trauma, pathol. conditions caused by the prodn. of bradykinin or related kinins, and in particular chronic inflammatory hyperalgesia contains an effective amt. of the said peptide to antagonize bradykinin and a suitable pharmaceutical carrier. Thus, title peptides. (I; Tic = tetrahydroisoquinoline-3-carboxylic acid, Oic = (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid), (II), and H-D-Arg-Arg-X[c-C6H11]-CH2CO-Ser-D-Tic-Oic-Arg-OH were manually synthesized by the std. solid phase method using Boc-Arg(Tos)-PAM resin and, in a radioligand binding assay, showed competitive binding to the human bradykinin B2 receptor against tritiated 3[H]NPC17731 (a bradykinin analog).

IT **168824-56-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide compds. as pseudo- and non-peptide bradykinin receptor antagonists)

L15 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:810933 HCAPLUS
DOCUMENT NUMBER: 124:56728
TITLE: Preparation of bradykinin antagonist pseudopeptide derivatives of olefinic aminoalkanoic acids
INVENTOR(S): Kyle, Donald J.
PATENT ASSIGNEE(S): Scios Nova, Inc., USA
SOURCE: U.S., 36 pp. Cont.-in-part of U.S. Ser. No.957,879.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 5444048	A	19950822	US 1993-118981	19930909	<--
US 5521158	A	19960528	US 1992-957879	19921008	<--
US 5541286	A	19960730	US 1994-281907	19940728	<--
CA 2171446	AA	19950316	CA 1994-2171446	19940909	<--
WO 9507294	A1	19950316	WO 1994-US10128	19940909	<--
W: CA, JP, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 716661	A1	19960619	EP 1994-929158	19940909	<--
EP 716661	B1	20000405			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 11500100	T2	19990106	JP 1994-508795	19940909	
AT 191486	E	20000415	AT 1994-929158	19940909	
ES 2148347	T3	20001016	ES 1994-929158	19940909	
US 5817756	A	19981006	US 1995-401595	19950309	
US 5610142	A	19970311	US 1995-416524	19950403	<--

PRIORITY APPLN. INFO.:

US 1992-957879	A2	19921008
US 1993-118550	A	19930909
US 1993-118558	A	19930909
US 1993-118981	A2	19930909
US 1993-119341	A	19930909
US 1994-281904	A	19940728
US 1994-281906	A	19940728
US 1994-281907	A	19940728
US 1994-281908	A	19940728
US 1994-119341	A	19940909
WO 1994-US10128	W	19940909
US 1994-353426	B2	19941209

OTHER SOURCE(S): MARPAT 124:56728
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Pseudopeptide compds. based on a modified bradykinin sequence having the formula A-B-C-D-E-F-G-R [A, B = L- or D-Arg or -Lys; C = Q - Q2, etc.; D = Ser, Thr, Gly, Ala, Val; E = D-Phe, tetrahydroisoquinoline-3-carboxylic acid residue (D-Tic), D-trans-Hype represented by D-trans-Q3; wherein R = H, (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkylalkyl, (un)substituted aryl, aralkyl, R1NHCO; wherein aryl is selected from Ph, naphthyl, CH2Ph, or naphthylmethyl; R1 = alkyl, aryl; X = O, S, SO, SO2; F = (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid (Oic), (S,S,S)-2-azabicyclo[3.3.0]octane-3-carboxylic acid (Aoc), Phe, Tic, Q3; G = Arg, Lys; R = OH, NH2, alkoxy], which have an affinity for bradykinin receptor and are potent bradykinin receptor antagonists and are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites, are prepd. Amino acids at positions 2 through 5 are replaced by olefinic aminoalkenoyl groups to reduce the peptidic nature of the compds. Thus, H-D-Arg-Arg-Q4-Ser-D-Tic-Oic-Arg-NH2 (I) was prepd. by the solid phase method using N-Boc-3-[2-(aminomethyl)phenyl]-2-propenoic acid, i.e. Boc-Q4-OH (prepn. given), N-Boc-protected amino acids, and Boc-Arg(Tos)-PAM resin. II showed binding affinity to human bradykinin receptor expressed in H20.2 cells and the bradykinin receptor in guinea pig terminal ileum with Ki value of 27 and 120.+-.8 nM, resp.

IT **168824-56-4P 171662-55-8P 171662-64-9P**
171662-73-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pseudopeptide derivs. contg. olefinic aminoalkanoic acids as bradykinin receptor antagonists)

L15 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:776761 HCAPLUS
DOCUMENT NUMBER: 124:9413
TITLE: Tripeptides as selective inhibitors of src-SH2 phosphoprotein interactions
AUTHOR(S): Rodriguez, Marc; Crosby, Renae; Alligood, Krystal; Gilmer, Tona; Berman, Judd
CORPORATE SOURCE: Glaxo Wellcome Res. Inst., Triangle Park, NC, 27709, USA
SOURCE: Letters in Peptide Science (**1995**), 2(1), 1-6
CODEN: LPSCEM; ISSN: 0929-5666
PUBLISHER: ESCOM
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis of phosphorylated peptides Ac-Tyr(PO3H2)-Glu-D-NHCHRCH2CH2CONH2 (I; R = CH2CH2Ph, Bu, 1-naphthylmethyl, 2-naphthylmethyl) as protein tyrosine kinase inhibitors is described. Peptides I displayed activities in the micromolar range in inhibiting src-SH2 domain/epidermal growth factor receptor interactions.

IT **171357-91-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of phosphotyrosine tripeptides as selective inhibitors of src-SH2 phosphoprotein interactions)

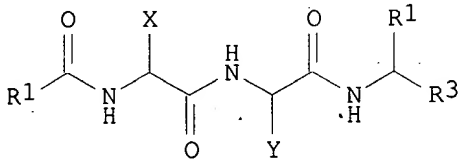
L15 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:667082 HCAPLUS

DOCUMENT NUMBER: 123:84007
TITLE: Preparation of peptideamide endothelin converting enzyme inhibitors.
INVENTOR(S): Leban, Johann Jakob; Sherman, Douglas Byron; Sigafoos, James Frederick; Spaltenstein, Andreas; Viveros, Osvaldo Humberto; Wan, David Chi-cheong
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

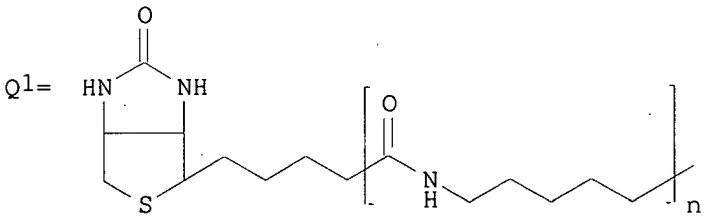
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9415956	A1	19940721	WO 1994-GB9	19940104 <--
W: AU, CA, CN, FI, HU, JP, KR, NO, NZ, PL, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
ZA 9400008	A	19950703	ZA 1994-8	19940103 <--
AU 9458202	A1	19940815	AU 1994-58202	19940104 <--
EP 677059	A1	19951018	EP 1994-903951	19940104 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08506569	T2	19960716	JP 1994-515796	19940104 <--
EP 1029869	A1	20000823	EP 2000-201447	19940104
EP 1029869	B1	20030423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 6235717	B1	20010522	US 1995-481365	19950703

PRIORITY APPLN. INFO.: GB 1993-48 A 19930104
EP 1994-903951 A3 19940104
WO 1994-GB9 W 19940104

OTHER SOURCE(S): MARPAT 123:84007
GI



I



AB Title compds. I; R1 = alkyl, carboxyalkyl, alkoxycarbonylalkyl, (substituted) aryl, aralkyl, aralkoxy, aryloxyalkyl, diphenylalkyl, Q1, R5CONH(CH2)5[Z(CH2)5]n, PhCH2O2CNHCH(CH2CO2R6); n = 0,1; Z = CONH, CH2; R5 = PhCH2O, 1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl, 2,5-dioxo-4-imidazolidinyl; R6 = H, alkyl; R2 = indol-3-ylmethyl, (substituted) aryl, aralkyl; R3 = CHO, maleimidomethyl, methoxycarbonylvinyl, dimethoxymethyl, semicarbaxonomethyl, alkyl, etc.; X = alkyl, indolylmethyl, naphthylmethyl, benzyloxybenzyl, cycloalkylmethyl, (substituted) PhCH2; Y = indolylmethyl, naphthylmethyl, benzyloxybenzyl, alkyl, (substituted) PhCH2, were prepd. Thus, N-[5-[(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-

4-yl)pentanoyl]-L-p-bromophenylalanyl-L-1-naphthylalanyl-L-N-[1-formyl]-2-(1H-indol-3-yl)ethyl]amide (soln. phase prepn. given) showed IC50 = 0.002 .mu.M in an endothelin converting enzyme asssay in porcine aortal prepns.

IT **164785-49-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptideamide endothelin converting enzyme inhibitors)

L15 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:183489 HCAPLUS
DOCUMENT NUMBER: 122:10659
TITLE: Cyclosporin A: Regioselective Ring Opening and Fragmentation Reactions via Thioamides. A Route to Semisynthetic Cyclosporins
AUTHOR(S): Eberle, Marcel K.; Jutzi-Eme, Anne-Marie; Nuninger, Francois
CORPORATE SOURCE: Preclinical Research, Sandoz Ltd., Basel, Switz.
SOURCE: Journal of Organic Chemistry (**1994**), 59(24), 7249-58
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:10659

AB Cyclosporin A served as the starting material for the semisynthetic prepn. of a variety of novel cyclosporins. Acetylcyclosporin A was treated with Lawesson's reagent. From the reaction mixt., three novel acetylated thioamides were isolated: the 4,7-bis(thioamide), the 7-thioamide, and the 4-thioamide. The acetylated products were hydrolyzed to the known thioamides. The 7-thioamide was alkylated to give the corresponding S-benzyl thioamidate. A regioselective ring opening reaction at the activated site was induced by treating the thioimidate under acidic conditions giving the 7,8-seco-cyclosporin. The D-Ala moiety was replaced by D-Phe via the Edman degrdn. product, and removal of the protecting groups led to the acyclic seco-cyclosporin. This was cyclized to [D-Phe]8-cyclosporin. An N-protected 7,8-seco-cyclosporin was reduced to the aldehyde, homologated, deprotected, and cyclized to give a vinylogous cyclosporin. Similarly, a 4,5-seco-cyclosporin was prepd. and converted via several steps to the vinylogous cyclosporin. Finally, under acidic conditions, a dibenzyl bis(thioamidate) underwent a fragmentation reaction to give the octapeptide and the tripeptide fragments. The octapeptide was coupled with a different tripeptide 9i and cyclized to give [L-Phe]7-cyclosporin.

IT **159392-00-4P 159392-01-5P 159392-02-6P**
159392-10-6P 159392-11-7P 159392-12-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of semisynthetic cyclosporins via regioselective ring opening and fragmentation reactions of thioamides)

L15 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:153723 HCAPLUS
DOCUMENT NUMBER: 120:153723
TITLE: Use of calpain inhibitors in the inhibition and treatment of medical conditions associated with increased calpain activity
INVENTOR(S): Eveleth, David D., Jr.; Lynch, Gary; Powers, James C.; Bartus, Raymond T.
PATENT ASSIGNEE(S): Cortex Pharmaceuticals, Inc., USA; Georgia Tech Research Corp.
SOURCE: PCT Int. Appl., 255 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9400095	A2	19940106	WO 1993-US6143	19930624	<--
WO 9400095	A3	19940317			

W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9345449	A1	19940124	AU 1993-45449	19930624	<--
JP 09500087	T2	19970107	JP 1993-502621	19930624	<--

PRIORITY APPLN. INFO.:
US 1992-903800 19920624
US 1993-34996 19930316
US 1993-72609 19930601
WO 1993-US6143 19930624

AB Medical conditions in mammals (e.g. cardiac muscle tissue damage, cataracts, smooth muscle damage, and vasospasm) assocd. with increased proteolytic activity of calpain are treated by administering a pharmaceutical compn. contg. a calpain inhibitor in a pharmacol. effective amt. The inhibitor is a peptide keto compd., substituted heterocyclic compd., or halo ketone peptide. Also, a method of inhibiting proliferation of smooth muscle cells and thereby preventing the restenosis of a blood vessel which has undergone therapeutic angioplasty includes the administration of a calpain inhibitor to the blood vessel during or after the angioplasty. Further, methods of blocking the establishment of the tonically contracted state in smooth muscle and relaxing tonically contracted smooth muscle are disclosed. These methods involve the administration of a calpain inhibitor, thereby reducing or preventing smooth muscle contraction assocd. with vasospasm and bronchospasm.

IT **153370-29-7 153370-30-0 153370-32-2**
RL: BIOL (Biological study)
(as calpain inhibitor, heart and vascular disease treatment with)

L15 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:77643 HCAPLUS
DOCUMENT NUMBER: 120:77643
TITLE: Preparation of tripeptides as cysteine protease inhibitors
INVENTOR(S): Tanami, Tooru; Yokoo, Chihiro; Hatayama, Katsuo
PATENT ASSIGNEE(S): Taisho Pharma Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
JP 05213990	A2	19930824	JP 1991-117054	19910227	<--

PRIORITY APPLN. INFO.:
JP 1991-117054 19910227

AB Me(CH2)nCH(OH)CH2COCNHCH(CH2CONH2)CONHCH(CH2CH2CONH2)CONHCH(CH2CHMe2)CHO (I; n = 11-15) are prepd. Boc-L-Asn-L-Gln-L-NHCH(CH2CHMe2)CH:CHCO2Et (Boc = CO2CMe3; prepn. given) (1.00 g) in HCl-dioxane was stirred at room temp. for 1 h and the reaction product was treated with 675 mg (.+-.)-3-hydroxypentadecanoic acid N-hydroxysuccinimide ester and NEt3 in DMF at 0.degree. for 1 h and at room temp. overnight to give 646 mg (.+-.)-Me(CH2)11CH(OH)CH2CO-L-Asn-L-Gln-L-NHCH(CH2CHMe2)CH:CHCO2Et, which (601 mg) was treated with O3 in CHCl3-MeOH at .apprx.-50.degree. for 20

min, mixed with Me2S, and stirred at -50.degree. to room temp. for 2 h to afford 538 mg (.+-.)-I (n = 11) (II). II had IC50 of 1400 nM against Ca-activated neutral protease.

IT **152338-63-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(ozonolysis of)

IT **152338-62-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and ozonolysis of)

IT **152378-15-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with hydroxypentadecanoate)

L15 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:148070 HCAPLUS
DOCUMENT NUMBER: 118:148070
TITLE: Preparation of tripeptide aldehyde derivatives as cysteine protease inhibitors
INVENTOR(S): Tanami, Toru; Yokoo, Chihiro; Hatayama, Katsuo
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04273897	A2	19920930	JP 1991-117056	19910227 <--

PRIORITY APPLN. INFO.: JP 1991-117056 19910227
OTHER SOURCE(S): MARPAT 118:148070

AB Me(CH2)nCH(OH)CH2CONHCH(CH2CONH2)CONHCH(CH2CH2CONH2)CONHCH(CHO)CH2CHMe2 (I; n = 4-6), useful for treatment of muscle degenerative diseases such as muscular dystrophy and vacuole-type distal myopathy, are prepd. Deprotection of 1.00 g Boc-Asn-Gln-NHCH(CH2CHMe2)CH:CHCO2Et (prepn. given) (Boc = CO2CMe3) by HCl/dioxane and condensation with 489 mg (.+-.)-3-hydroxyoctanoic acid N-hydroxysuccinimide ester in Et3N/DMF gave 632 mg (.+-.)-Me(CH2)4CH(OH)CH2CO-Asn-Gln-NHCH(CH2CHMe2)CH:CHCO2Et, 570 mg of which was treated with O3 in CHCl3/MeOH at -50.degree. for 20 min and stirred with Me2S for 2 h to give 500 mg (.+-.)-I (n = 4) (II). II in vitro inhibited calpain I, papain, and cathepsin B with IC50 of 1200, 12,400, and 1800 nM, resp.

IT **146508-92-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(ozonization of, in prepn. of cysteine protease inhibitors)

IT **146026-89-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and amidation of, with hydroxyalkanoate)

IT **146508-90-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and ozonization of, in prepn. of cysteine protease inhibitors)

L15 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:148069 HCAPLUS
DOCUMENT NUMBER: 118:148069
TITLE: Preparation of tripeptide aldehyde derivatives as cysteine protease inhibitors
INVENTOR(S): Tanami, Toru; Yokoo, Chihiro; Hatayama, Katsuo

PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04273896	A2	19920930	JP 1991-117055	19910227 <--

PRIORITY APPLN. INFO.: JP 1991-117055 19910227
OTHER SOURCE(S): MARPAT 118:148069
AB Me(CH2)9CH(OH)(CH2)nCONHCH(CH2CONH2)CONHCH(CH2CH2CONH2)CONHCH(CHO)CH2CHMe2 (I; n = 0, 1), useful for treatment of muscle degenerative diseases such as muscular dystrophy and vacuole-type distal myopathy, are prepd. Deprotection of 1.00 g Boc-Asn-Gln-NHCH(CH2CHMe2)CH:CHCO2Et (prepn. given) (Boc = CO2CMe3) by HCl/dioxane and condensation with 622 mg (.+-.)-3-hydroxytridecanoic acid N-hydroxysuccinimide ester in Et3N/DMF gave 648 mg (.+-.)-Me(CH2)9CH(OH)CH2CO-Asn-Gln-NHCH(CH2CHMe2)CH:CHCO2Et, 576 mg of which was treated with O3 in CHCl3/MeOH at -50.degree. for 20 min and stirred with Me2S for 2 h to give 513 mg (.+-.)-I (n = 1) (II). II in vitro inhibited calpain I, papain, and cathepsin B with IC50 of 510, 40,400, and 14,900 nM, resp.
IT **146508-96-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(ozonization of, in prepn. of cysteine protease inhibitors)
IT **146026-89-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and amidation of, with hydroxyalkanoate)
IT **146508-94-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and ozonization of, in prepn. of cysteine protease inhibitors)

L15 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:125001 HCAPLUS
DOCUMENT NUMBER: 118:125001
TITLE: Stereoselective nucleophilic addition reactions of reactive pseudopeptides
AUTHOR(S): Reetz, Manfred T.; Kanand, Juergen; Griebenow, Nils; Harms, Klaus
CORPORATE SOURCE: Max-Planck-Inst. Kohlenforsch., Muelheim an der Ruhr, W-4330, Germany
SOURCE: Angewandte Chemie (**1992**), 104(12), 1638-41
(See also Angew. Chem., Int. Ed. Engl., 1992, 31(12), 1626-9)
CODEN: ANCEAD; ISSN: 0044-8249
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 118:125001
GI For diagram(s), see printed CA Issue.
AB Stereoselective Michael addn. reactions of cuprates R2CuLi (R = Me, Me3C) to alkene pseudopeptides I (R = Boc-Ala, Boc-D-Ala, Boc-Phe, Boc-D-Phe, Boc-Phe-Ala, Boc-D-Phe-Ala; Boc = Me3CO2C) in the presence of Me3SiCl gave predominantly or exclusively adducts II. Similarly, addn. of Me2CuLi to leucinal derivs. R2-L-Leu-H (III; R2 = Z-Ala, Z-D-Ala, Z-Phe, Z-D-Phe; Z = PhCH2O2C) gave predominantly or exclusively adducts IV. A doubly chelated Cu(I) intermediate is postulated to explain the stereoselectivity of the cuprate addns. to III.
IT **144345-56-2P 144408-31-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(prepn. and Michael addn. reactions of, with cuprates, stereochem. of)

L15 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:102476 HCAPLUS
DOCUMENT NUMBER: 118:102476
TITLE: Preparation of tripeptide aldehyde derivatives as protease inhibitors.
INVENTOR(S): Tanami, Toru; Yokoo, Chihiro; Hatayama, Katsuo
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04202170	A2	19920722	JP 1990-332085	19901129 <--

PRIORITY APPLN. INFO.: JP 1990-332085 19901129
AB RNHCH(CH2R1)CONR2(CH2)nCR3R4CONHCHR5CHO [R = H, protecting group; R1 = (protected) CO2H, H2NCO; R2, R3 = H, alkyl; R2R3 = (CH2)3; R4 = H, alkyl, PhCH2, etc., R3R4 = (CH2)4; R5 = isobutyl; n = 0, 1], useful as cysteine protease inhibitors for treating muscular dystrophy, etc., were prepd. Boc-Asp(OBzl)-OSu (Su = succinimidyl) was stirred with valylleucinol in EtOAc under cooling to give coupling product which in Et3N/Me2SO was treated with pyridine-SO3 under cooling to give Boc-Asp(OBzl)-Val-Leu-H. Boc-Asp(OBzl)-Ser(Bzl)-Leu-H showed IC50 of 987, 95, and 987 (no units given) against Ca-dependent neutral protease, papain, and cathepsin b, resp., vs. 2000, 30,000, and 7300, resp., with a ref. compd.
IT **146026-89-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of cysteine protease inhibitor)

L15 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:81438 HCAPLUS
DOCUMENT NUMBER: 118:81438
TITLE: Peptide keto amides, keto acids, and keto esters
INVENTOR(S): Powers, James C.
PATENT ASSIGNEE(S): Georgia Tech Research Corp., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9212140	A1	19920723	WO 1991-US9801	19911227 <--
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MW, NL, NO, PL, RO, RU, SD, SE				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2098702	AA	19920629	CA 1991-2098702	19911227 <--
AU 9191553	A1	19920817	AU 1991-91553	19911227 <--
AU 654834	B2	19941124		
EP 564561	A1	19931013	EP 1992-903265	19911227 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL				

PRIORITY APPLN. INFO.: US 1990-635287 19901228
WO 1991-US9801 19911227

OTHER SOURCE(S): MARPAT 118:81438

AB Title compds. R-X-X1-COR1 [X, X1 = amino acids; R = H, (un)substituted H2NCO, H2NCS, H2NSO2, amino acid; R1 = alkoxy, OH, (un)substituted NH2] were prepd. as serine and cysteine protease inhibitors. Thus, Z-Leu-Phe-OH (Z = CO2CH2Ph) was treated with ClCOCO2Et in the presence of 4-dimethylaminopyridine to give Z-Leu-NHC(CH2Ph)=C(CO2Et)O2CCO2Et which was hydrolyzed to 2-Leu-Phe-CO2Et. The latter compd. was ketalized and amidated with EtNH2, to give Z-Leu-Phe-CONHEt (I). I inhibited calpain from humor erythrocytes at 7 .mu.m.

IT **145731-18-6P 145731-19-7P 145731-21-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrolysis of)

L15 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:822 HCAPLUS
DOCUMENT NUMBER: 118:822
TITLE: Use of calpain inhibitors in the inhibition and treatment of neurodegeneration
INVENTOR(S): Bartus, Raymond T.; Eveleth, David D., Jr.; Lynch, Gary S.; Powers, James C.
PATENT ASSIGNEE(S): Cortex Pharmaceuticals, Inc., USA; Georgia Tech Research Corp.
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9211850	A2	19920723	WO 1991-US9786	19911227 <--
WO 9211850	A3	19920903		
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2098609	AA	19920629	CA 1991-2098609	19911227 <--
AU 9191527	A1	19920817	AU 1991-91527	19911227 <--
AU 667463	B2	19960328		
EP 564552	A1	19931013	EP 1992-902904	19911227 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06504061	T2	19940512	JP 1991-503767	19911227 <--
US 5444042	A	19950822	US 1994-207881	19940307 <--
AU 9655905	A1	19960822	AU 1996-55905	19960611 <--
AU 9923782	A1	19990603	AU 1999-23782	19990415

PRIORITY APPLN. INFO.:
US 1990-635952 19901228
US 1991-682925 19910409
US 1991-816120 19911227
WO 1991-US9786 19911227
AU 1996-55905 19960611

OTHER SOURCE(S): MARPAT 118:822

AB Calpain inhibitors such as isocoumarins, substituted heterocyclic compds., and peptide keto compds., are used in the treatment of neurodegeneration. Examples are given for the synthesis of a large no. of these compds. Data are also given showing protease inhibition by halo-ketone peptides, inhibition of calpain in crude brain exts. by calpain inhibitors, in vivo protection against neurodegeneration, membrane permeation of calpain inhibitors, screens for inhibition of anoxic damage, and protection against spectrin breakdown from excitotoxic damage by peripherally administered calpain inhibitors. A neuorprotective compn. for i.v. drip was prepd. contg. Z-Leu-Phe-CONHEt.

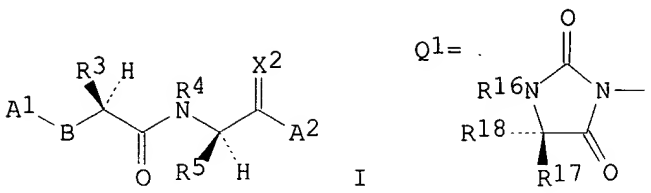
IT **144231-95-8P 144231-96-9P 144231-97-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and isomerization of)

L15 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:256053 HCAPLUS
DOCUMENT NUMBER: 116:256053
TITLE: Preparation of endothelin antagonistic peptide derivatives
INVENTOR(S): Ishikawa, Kiyofumi; Fukami, Takehiro; Hayama, Takashi; Niiyama, Kenji; Nagase, Toshio; Mase, Toshiaki; Fujita, Kagari; Ihara, Masaki; Ikemoto, Fumihiko; Yano, Mitsuo
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 121 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

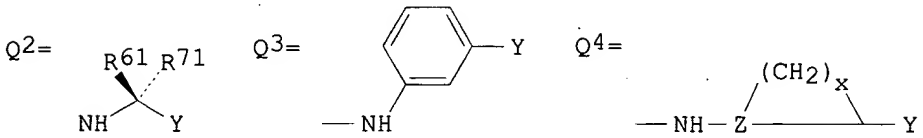
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 460679	A2	19911211	EP 1991-109313	19910606	<--
EP 460679	A3	19921119			
EP 460679	B1	19981028			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
CA 2043741	AA	19911208	CA 1991-2043741	19910603	<--
JP 05178891	A2	19930720	JP 1991-160023	19910603	<--
JP 3127488	B2	20010122			
AU 9178182	A1	19911212	AU 1991-78182	19910605	<--
AU 632695	B2	19930107			
AT 172741	E	19981115	AT 1991-109313	19910606	
US 5470833	A	19951128	US 1994-213829	19940314	<--
US 5691315	A	19971125	US 1995-494818	19950626	<--

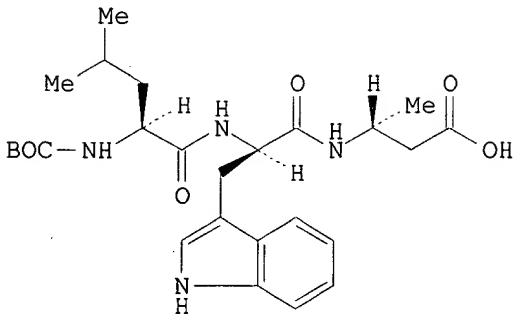
PRIORITY APPLN. INFO.:
JP 1990-149105 A 19900607
US 1991-712095 B3 19910607
US 1992-884189 B1 19920518
US 1994-213829 A3 19940314

OTHER SOURCE(S): MARPAT 116:256053
GI



I





II

AB Title compds. [I; A1 = (cyclo)alkylcarbonyl, aryl, arylalkyl, 1,3-dithiol-2-ylidenemethyl, alkoxycarbonyl, phenoxycarbonyl, (thio)carbamoyl, etc.; A1B = Q1; R16 = H, (cyclo)alkyl; R17, R18 = H, alkyl; B = O, NH, NMe; R3 = alkyl; R4 = H, Me; R5 = (substituted) 3-indolylmethyl, (2,3-dihydro-2-oxo-3-indolyl)methyl, phosphonyl(alkyl), PhCH2, 3-benzothienylmethyl, etc.; X2 = O, S; A2 = Q2, Q3, Q4, etc.; Y = sulfo, phosphono, CO2H, alkoxycarbonyl, benzyloxycarbonyl, carbamoyl; R61 = H, alkyl; R71 = H, (substituted) alkyl; R61R71 = CH2; Z = CH, N; x = 1-3], were prepd. BOC-Leu-OH was coupled with H-D-Trp-OMe.HCl using Et3N/hydroxybenzotriazole/1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in CH2Cl2 and the product was treated with N2H4 in DMF to give BOC-Leu-D-Trp-NHNH2. The latter in DMF at -60.degree. was treated with HCl/dioxane, isoamyl nitrite, and tetrabutylammonium 3R-aminobutanoate to give title compd. II. I inhibited 125I-endothelin binding to porcine aortal prepns. by 20-90%, and effectively inhibited endothelin-induced contraction of porcine coronary artery and guinea pig trachea.

IT **141595-35-9P 141661-07-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as endothelin antagonist)

L15 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:106810 HCAPLUS
DOCUMENT NUMBER: 116:106810
TITLE: Preparation of .beta.-chloro-Z-dehydroglutamic acid-containing peptides as bactericides
INVENTOR(S): Morita, Yoshiharu; Ando, Ryoichi; Takashima, Junko; Chaiet, Louis
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5041644	A	19910820	US 1988-211618	19880627 <--

PRIORITY APPLN. INFO.: US 1988-211618 19880627
OTHER SOURCE(S): MARPAT 116:106810

AB Title compds. (Z)-XNHCH[ClC:CH(COR)]COY [X = H, amino acid or peptide residue; Y, R = (protected) OH, (C-terminal protected) amino acid or (terminal protected) peptide residue; with proviso] were prepd. as medical bactericides (no data). Thus, .beta.-chloro-L-(Z)-dehydroglutamic acid and BOC-Ala-OH hydroxysuccinimide ester were coupled in EtOH contg. aq. NaHCO3 and the resulting Boc-protected dipeptide was deprotected by HBr in HOAc to give, after neutralization of the hydrobromide salt, L-alanyl-.beta.-chloro-L-(Z)-dehydroglutamic acid.

IT **121931-73-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for medical bactericide)

IT **121931-66-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as medical bactericide)

L15 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:509294 HCAPLUS
DOCUMENT NUMBER: 115:109294
TITLE: Studies on the binding of pepstatin and its derivatives to Rhizopus pepsin by quantum mechanics, molecular mechanics, and free energy perturbation methods
AUTHOR(S): Rao, B. G.; Singh, U. Chandra
CORPORATE SOURCE: Dep. Mol. Biol., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (**1991**), 113(18), 6735-50
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ab initio quantum mechanics, mol. mechanics, and free energy perturbation methods have been applied to study the energetics of the active site of Rhizopus pepsin and its interactions with several inhibitors derived from pepstatin. The studies on the aspartate (Asp) dyad in the active site of the enzyme show that the energetics of the dyad are very sensitive to small changes in the relative orientations of the dyad and hence the energetic equivalence of the two charge states of the dyad (arising due to the protonation of either of the two aspartates) can be easily attained by small changes in the at. positions of the dyad. Further, the proton may shuttle between the two inner oxygens of the dyad. The barrier for the proton shuttle could be as low as 1.0 kcal/mol when the inner oxygen distance is .apprx.2.5 .ANG. and it increases with increases in this distance. Although the present studies show that the configurations of the Asp dyad distorted from planarity are lower in energy than the coplanar configuration found in the crystal structure, the latter configuration is crucial for optimal inhibitor binding. This is also borne out in the calcd. binding free energy differences between pepstatin and its derivs. The calcd. values obtained with the lower energy configuration of the Asp dyad were lower than those obtained with the Asp dyad configuration found in the crystal structure, and the latter values were closer to the exptl. results. For the mutation of the central statine residue of pepstatin to dehydroxystatine, the calcd. free energy difference of 5.17 kcal/mol is in good agreement with the exptl. value. This shows that the contribution of about 5 kcal/mol to binding from the

hydroxyl group of the central statine residue is mainly due to the strong interaction of this group with the neg. charged Asp dyad. The results of the other mutations on pepstatin also support this view.

IT **134486-20-7**
RL: BIOL (Biological study)
(binding of, by pepsin of Rhizopus, modeling of, by quantum mechanics and mol. mechanics and free energy perturbation methods)

L15 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:247788 HCAPLUS
DOCUMENT NUMBER: 114:247788
TITLE: Peptide derivatives preparation as retroviral protease inhibitors
INVENTOR(S): Kempf, Dale J.; Plattner, Jacob J.; Norbeck, Daniel W.; Boyd, Steven A.; Baker, William R.; Erickson, John W.; Fung, Anthony K. L.; Crowley, Steven R.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8910752	A1	19891116	WO 1989-US2055	19890512 <--
W: AU, DK, JP, KR, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
EP 342541	A2	19891123	EP 1989-108590	19890512 <--
EP 342541	A3	19911106		
R: ES, GR				
AU 8935660	A1	19891129	AU 1989-35660	19890512 <--
EP 415981	A1	19910313	EP 1989-905856	19890512 <--
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 03504247	T2	19910919	JP 1989-506033	19890512 <--

PRIORITY APPLN. INFO.: US 1988-194678 19880513
WO 1989-US2055 19890512

OTHER SOURCE(S): MARPAT 114:247788

AB Peptide derivs. are prepd. as retroviral protease inhibitors. Synthetic processess involved carbodiimide coupling, or coupling in combination with deprotection, and reaction with mixed anhydrides. Thus, N-methyl-1-cyclohexenecarboxamide was treated with BuLi in THF, treated with ClTi(OPr-iso)3, and then Boc-phenylalaninal to give N-methyl-6-[2-(tert-butoxycarbonyl)amino-1-hydroxy-3-phenyl]propyl-1-cyclohexenecarboxamide. This was then deprotected with HCl in dioxane to give N-methyl-6-(2-amino-1-hydroxy-3-phenylpropyl)-1-cyclohexenecarboxamide-HCl (I). I was coupled with Boc-Leu-Asn in the presence of 180-BuO2CCl to give the amide.

IT **129740-82-5P 129740-98-3P 130216-63-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L15 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:478603 HCAPLUS
DOCUMENT NUMBER: 111:78603
TITLE: Preparation of peptide derivatives of .beta.-chloro-L-(Z)-dehydroglutamic acid as antibacterials
INVENTOR(S): Morita, Yoshimi; Ando, Ryoichi; Takashima, Junko
PATENT ASSIGNEE(S): Mitsubishi Kasei Corp., Japan; Merck and Co., Inc.
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01013065	A2	19890117	JP 1987-166938	19870706 <--

PRIORITY APPLN. INFO.: JP 1987-166938 19870706
OTHER SOURCE(S): MARPAT 111:78603
AB Peptides contg. .beta.-chloro-L-(Z)-dehydroglutamic acid represented by (Z)-XNHCH(COY)CCl:CHCOZ [I; X = H, C-terminus residue of amino acid or peptide; Y, Z = (un)protected HO or N-terminus residue of amino acid or peptide optionally protected at CO2H group with same or different protective group; excluding the case where X = H and Y = Z = protected HO] were prepd. as antibacterials (no data). A soln. of .beta.-chloro-L-(Z)-dehydroglutamic acid and N-tert-butoxycarbonyl-L-alanine hydroxysuccinimide ester in EtOH and 0.3M aq. NaHCO3 was stirred overnight to give 81% BOC-Ala-L-(Z)-NHCH(CO2H)CCl:CHCO2H (BOC = Me3CO2C) which was treated 15 min at room temp. with HBr-satd. AcOH to give, after treatment with propylene oxide in EtOH, H-Ala-L-(Z)-NHCH(CO2H)CCl:CHCO2H.
IT **121931-73-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and N-deprotection of)
IT **121931-66-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as antibacterial)

L15 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:439861 HCAPLUS
DOCUMENT NUMBER: 111:39861
TITLE: Preparation of peptides as renin inhibitors
INVENTOR(S): Hudspeth, James P.; Kaltenbronn, James S.; Lunney, Elizabeth A.; Repine, Joseph T.; Roark, W. Howard; Stier, Michael A.; Tinney, Francis J.; Woo, Peter W. K.; Nicolaides, Ernest D.
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: U.S., 64 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4743585	A	19880510	US 1986-920330	19861121 <--
WO 8803927	A2	19880602	WO 1987-US2820	19871021 <--
WO 8803927	A3	19880811		
W: AU, BB, BG, BR, DK, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8783361	A1	19880616	AU 1987-83361	19871021 <--

PRIORITY APPLN. INFO.: US 1986-920330 19861121
WO 1987-US2820 19871021
OTHER SOURCE(S): MARPAT 111:39861
AB R-X-An-Y-Bn-T-Cn-W-Dn-V-En-U [I; n = 0, 1, the compd. must contain .gtoreq.1 link where n = 1; R = CO2CMe3, CO2CH2Ph, valeryl, isovaleryl, isobutyryl, Bz, HO2C(CH2)3CO, Me3CCO; X = Phe, Trp, cyclohexyl-Ala, 1-naphthyl-Ala, homo-Phe, Phe(Me5), Val, Ile, Leu; Y = bond, Phe, His, His(CH2OCH2Ph), Gly, phenyl-Gly, Leu, Val, Ile, Orn, Orn(phthaloyl), Arg,

Arg(NO2); T = sta, benztine or cyclotine residue, Leu, cyclohexyl-Ala, Phe; W = bond, Leu, Gly, Ile; V = bond, Leu, Ile; U = NHCH2Ph, NHCH2C6H4(CH2NHCO2CH2Ph)-3, NH2, OMe, OEt, etc.; A = CH2NH, CH2NOH, CH2S, CH2SO, CH:CH, CH(OH)CH2, CH(OH)CH(OH), COCH2, etc.; B = CH2NH; C = CH2NH, CH(OH)CH2, CH(OH)CH:CHCH2; D = CH2NH; E = CH2NH, CH2NHCO2CH2Ph], useful for treatment of renin-assocd. hypertension and hyperaldosteronism, were prepd. A soln. of 0.5 H-Sta-Ala-Sta-NHCH2Ph, 0.5 [S-(E)]-5-[[(1,1-dimethylethoxy)carbonyl]amino]-6-phenyl-3-hexenoic acid, and 0.5 mmol 1-hydroxybenzotriazole in DMF was cooled in ice and treated with a soln. of dicyclohexylcarbodiimide in DMF. After 1 h at 0.degree., the mixt. was stirred at room temp. overnight to give 240 mg [5S-[5R,6R,9R,13R,14R-(E),20R]]-20-benzyl-3,8,11,16-tetraoxo-1-phenyl-2,7,10,15,21-pentaazadocos-18-en-22-oic acid 1,1-dimethylethyl ester [BOC-Phe[CH=CH]Gly-Sta-Ala-Sta-NHCH2Ph] (BOC = CO2CMe3). I in vitro inhibited renin with IC50 of 1.4 .times. 10-8 to 6.3 .times. 10-5 M.

IT **118405-39-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. of, as renin-inhibiting antihypertensive)

L15 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1989:76077 HCAPLUS

DOCUMENT NUMBER: 110:76077

TITLE: Preparation and testing of peptidylaminohydroxyalkenoates as renin inhibitors

INVENTOR(S): Tanaka, Seiichi; Koike, Yutaka; Nakano, Masato; Atsuumi, Shugo; Morishima, Hajime; Matsuyama, Kenji

PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 272583	A2	19880629	EP 1987-118570	19871215 <--
EP 272583	A3	19900110		
EP 272583	B1	19930915		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 63270649	A2	19881108	JP 1987-313886	19871211 <--
AT 94559	E	19931015	AT 1987-118570	19871215 <--
US 4927565	A	19900522	US 1987-133642	19871216 <--

PRIORITY APPLN. INFO.:
JP 1986-301596 19861219
JP 1987-313886 19871211
EP 1987-118570 19871215

OTHER SOURCE(S): MARPAT 110:76077

AB R1(NR2CHR3CO)n(NHCHR4CO)mNR5CHR6CH(OH)CH:CR7COR8 [I; R1, R2 = H, aralkyl, alkoxycarbonyl, aryloxycarbonyl, or alkyloxycarbonyl, (substituted) alkanoyl, carbamoyl; R3, R4, R6 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, amino acid residue; R5 = H, alkyl; R7 = H, alkyl, cycloalkyl, cycloalkylalkyl, (substituted) aralkyl; R8 = OH, alkoxy, aryloxy, aralkoxy, etc.; m, n = 0, 1] and their salts, useful as antihypertensives, were prepd. L-Benzyloxycarbonylnaphthylalanyl-L-norleucine hydrazide in DMF/dioxane/HCl at -60.degree. was treated with isoamyl nitrite; the temp. was raised to -20.degree., brought back to -60.degree., and N-methylmorpholine and 4S,5S-5-amino-4-hydroxy-7-methyl-2(E)-octenoic acid isobutylamide were added. The mixt. was stirred overnight at 8.degree. to give 4S,5S-5-(L-N-benzyloxycarbonylnaphthylalanyl-L-norleucyl)amino-4-hydroxy-7-methyl-2(E)-octenoic acid isobutylamide. I inhibited human plasma renin with IC50's of 14 .times. 10-6 - 1.9

.times. 10-8 M.

IT **118741-32-5P 118741-33-6P 118741-34-7P**
118741-40-5P 118741-41-6P 118741-42-7P
118741-43-8P 118741-44-9P 118741-45-0P
118779-12-7P 118865-57-9P 118865-58-0P
118865-59-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as renin inhibitor)

IT **118741-02-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as renin inhibitor intermediate)

L15 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:423372 HCAPLUS
DOCUMENT NUMBER: 109:23372
TITLE: Synthesis and renin inhibitory activity of angiotensinogen analogs having dehydrostatine, Lue.psi.[CH2S]Val, or Lue.psi.[CH2SO] Val at the Pt, P1' cleavage site
AUTHOR(S): Smith, Clark W.; Saneii, Hossain H.; Sawyer, Tomi K.; Pals, Donald T.; Scahill, Terrence A.; Kamdar, Bharat V.; Lawson, Judy A.
CORPORATE SOURCE: Biopolym. Chem. Unit, Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Journal of Medicinal Chemistry (**1988**), 31(7), 1377-82
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:23372

AB Title angiotensinogen analogs H-Pro-His-Pro-Phe-His-Dhs-Ile-D-Lys-OH (I, Dhs = dehydrostatine residue), H-Pro-His-Pro-Phe-His-Leu.psi.[CH2S]Val-Ile-His-D-Lys-OH (.psi.[CH2S] = replacement of CONH with CH2S), and the corresponding Leu.psi.[CH2SO]Val peptide were prepd. and their in vitro renin-inhibiting potencies were detd. The above peptides were compared to the corresponding statine (Sta), Leu.psi.[CH2NH]Val, and Phe-Phe analogs. The Dhs pseudodipeptide was an adequate mimic of a trans CONH bond; I was approx. equal in potency to a Phe-Phe-contg. inhibitor, but 100-fold less potent than its Sta-substituted congener. That the enhanced potency of the Sta-contg. peptide most likely depends on H bonding as well as tetrahedral geometry is indicated by the 100-fold lower potency of the tetrahedral Leu.psi.[CH2-S]Val and Leu.psi.[CH2SO]Val analogs as compared to the Leu.psi.[CH2NH]Val-contg. congener.

IT **114423-48-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and renin-inhibiting activity of)

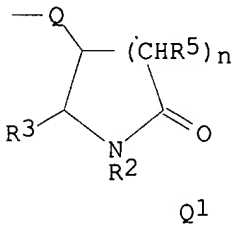
L15 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:554753 HCAPLUS
DOCUMENT NUMBER: 107:154753
TITLE: Renin-inhibiting peptides for treatment of hypertension and aldosteronism
INVENTOR(S): Raddatz, Peter; Hoelzemann, Guenter; Jonczyk, Alfred; Schmitges, Claus J.; Minck, Klaus Otto; Radunz, Hans Eckart; Sombroek, Johannes
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Fed. Rep. Ger.
SOURCE: Ger. Offen., 43 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3512128	A1	19861009	DE 1985-3512128	19850403 <--
EP 198271	A2	19861022	EP 1986-103944	19860322 <--
EP 198271	A3	19900228		
EP 198271	B1	19930609		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
AT 90359	E	19930615	AT 1986-103944	19860322 <--
AU 8655302	A1	19861009	AU 1986-55302	19860326 <--
AU 591892	B2	19891221		
HU 42102	A2	19870629	HU 1986-1409	19860401 <--
HU 201776	B	19901228		
CA 1276390	A1	19901113	CA 1986-505553	19860401 <--
JP 61229851	A2	19861014	JP 1986-75635	19860403 <--
ZA 8602484	A	19861126	ZA 1986-2484	19860403 <--
ES 553691	A1	19870801	ES 1986-553691	19860403 <--
US 4755592	A	19880705	US 1986-847977	19860403 <--

PRIORITY APPLN. INFO.: DE 1985-3512128 19850403
EP 1986-103944 19860322

OTHER SOURCE(S): CASREACT 107:154753
GI



Q1

AB X-Z-W-E-W1-Y [X = H, R1O(CH2)nCO, R1(CH2)nO2C, R1SO2, (9-fluorenylalkyoxy)carbonyl, etc.; Z = 0-4 amino acid residues chosen from Ala, Arg, Asn, Gln, ILe, Lys, Orn, Pro, Val, etc.; W, W1 = NR2CHR3CHR4(CHR5)nCO; E = 0-2 amino acid residues chosen from Abu (2-aminobutanoic acid), Ala, ILe, Leu, Met, Nle, Val; Y = O(CH2)t R6, NH(CH2)tR6, amino; W1 - Y = Q1; R1, R3 = alkyl, aryl, (substituted) cycloalkyl, etc.; Ri, R5, R6 = H, alkyl; R4 = OH, NH2; Q = O, NH; n,t = 0-5, r = 1,2] (I) were prepd. as renin inhibitors useful for the treatment of hypertension and aldosteronism (no data). Thus, Me 3-oxo-4(S)-[3(S)-hydroxy-4(S)-(tert-butoxycarbonylphenylalanylhistidylstatylisoleucyl]-6-methylheptanoate was oximated and hydrogenated to give BOC-Phe-His-Sta-Ile-DAMH-OMe [DAMH = NHCN(CH2CHMe2)CH(NH2)CH2CO] (II). A soln. for injection was prepd. contg. 100 g II and 5 g Na2HPO4 in 3 L H2O, the mixt. being brought to pH 6.5 with 2 N HCl.

IT **109291-95-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with benzylamine)

L15 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:553553 HCAPLUS
DOCUMENT NUMBER: 105:153553
TITLE: Diamino acid derivatives
INVENTOR(S): Raddatz, Peter; Schmitges, Claus
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Fed. Rep. Ger.
SOURCE: Ger. Offen., 33 pp.

CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 3418491	A1	19851121	DE 1984-3418491	19840518	<--
EP 161588	A2	19851121	EP 1985-105391	19850503	<--
EP 161588	A3	19870616			
EP 161588	B1	19900816			
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE					
AT 55612	E	19900915	AT 1985-105391	19850503	<--
AU 8542285	A1	19851121	AU 1985-42285	19850510	<--
AU 587186	B2	19890810			
CA 1268597	A1	19900501	CA 1985-481660	19850516	<--
ES 543258	A1	19860101	ES 1985-543258	19850517	<--
JP 61017546	A2	19860125	JP 1985-104118	19850517	<--
ZA 8503762	A	19860129	ZA 1985-3762	19850517	<--
HU 40072	A2	19861128	HU 1985-1867	19850517	<--
HU 200478	B	19900628			
US 4666888	A	19870519	US 1985-735247	19850517	<--
US 4746649	A	19880524	US 1987-33366	19870402	<--

PRIORITY APPLN. INFO.: DE 1984-3418491 19840518
EP 1985-105391 19850503
US 1985-735247 19850517

OTHER SOURCE(S): CASREACT 105:153553

AB R-Z-NHCH(CH2R1)CH(NH2)CH2CO-Z1-Z2-R2 [I; R = H, R3OCH2CO, R3O2C, R3(CH2)n CO where R3 = alkyl and n = 0-5; R1 = H, alkyl, cycloalkyl, aryl; R2 = (un)substituted alkyloxy, (un)substituted alkylamino, (un)substituted amino; Z = a chain contg. 0-4 amino acid residues; Z1 = --, Ala, Gly, Ile, Leu, Met, Ser, Thr, Val; Z2 = His, Phe, Trp, Tyr, NHCH(CH2R1)CH(NH2)CH2CO], useful as antihypertensives and hyperaldosteronism inhibitors (no data), were prepd. Thus, (4S)-Me2CHCH2CH(NHCO2CMe3)COCH2CO2Me in MeOH contg. NH4OAc was treated with Na(CN)BH3 at 20.degree. for 12 h to give a mixt. of (3S, 4S)- and (3R, 4S)- Me2CHCH2CH(NHCO2CMe3)CH(NH2)CH2CO2Me. Coupling of (3S)-FMOC-amino-(4S)-BOC-amino-6-methylheptanoic acid (FMOC = 9-fluorenylmethoxycarbonyl; BOC = tert-butoxycarbonyl) with the appropriate protected amino acids gave, after deprotection and treatment with HCl, I (R = H; R1 = Me2CH; R2 = NH2; Z = His-Pro-Phe-His; Z1 = Ile; Z2 = Phe) HCl (II). An injection was prepd. from 1 kg II, 50 g Na2HPO4 and 30 L H2O (pH adjusted to 6.5 with 2N HCl).

IT **104021-75-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of)

=> select hit rn l15 1-31
E1 THROUGH E199 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 14:31:59 ON 29 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 MAY 2003 HIGHEST RN 521913-14-4

DICTIONARY FILE UPDATES: 28 MAY 2003 HIGHEST RN 521913-14-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
=>

=> d his l16

(FILE 'HCAPLUS' ENTERED AT 14:30:55 ON 29 MAY 2003)
SELECT HIT RN L15 1-31

FILE 'REGISTRY' ENTERED AT 14:31:59 ON 29 MAY 2003
L16 199 S E1-E199

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L16  ANSWER 1 OF 199  REGISTRY  COPYRIGHT 2003 ACS
RN   199007-58-4  REGISTRY
CN   L-Phenylalaninamide, N-[4-[(methylamino)carbonyl]benzoyl]-L-leucyl-N-
     [(1S,2E)-1-(3-amino-3-oxopropyl)-4-ethoxy-4-oxo-2-butenyl]- (9CI)  (CA
     INDEX NAME)
FS   STEREOSEARCH
MF   C33 H43 N5 O7
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.
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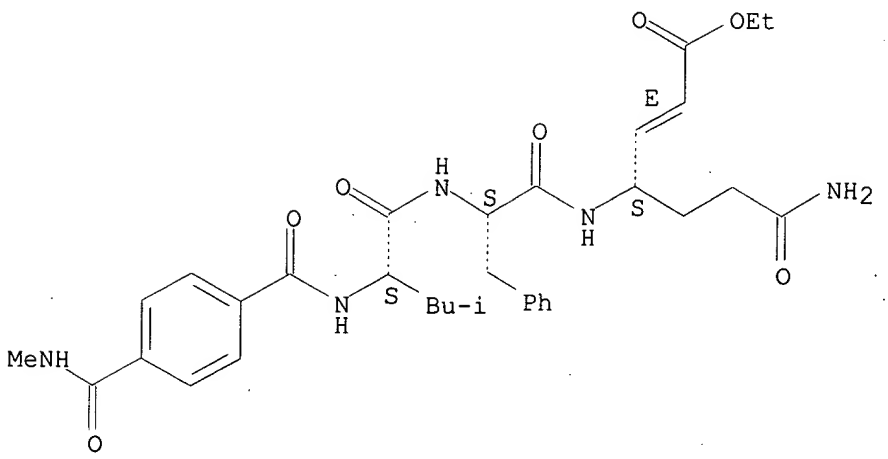


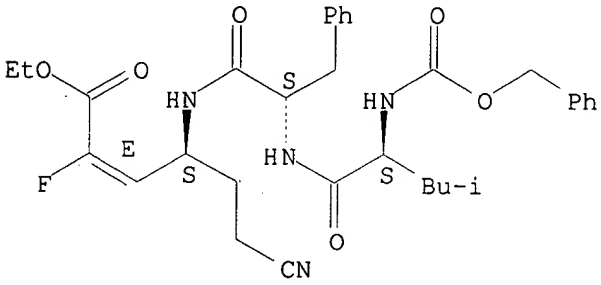
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 128:13442

L16 ANSWER 2 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **199006-67-2** REGISTRY
CN L-Phenylalaninamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S,2E)-1-(2-cyanoethyl)-4-ethoxy-3-fluoro-4-oxo-2-butenyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H39 F N4 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



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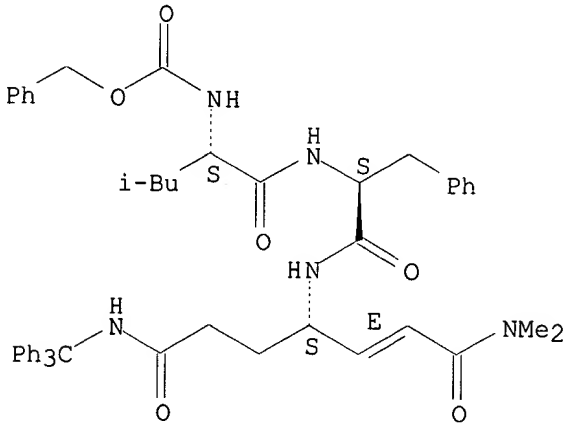
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 128:13442

L16 ANSWER 16 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **199005-84-0** REGISTRY
CN L-Phenylalaninamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S,2E)-4-(dimethylamino)-4-oxo-1-[3-oxo-3-[(triphenylmethyl)amino]propyl]-2-

butenyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C51 H57 N5 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



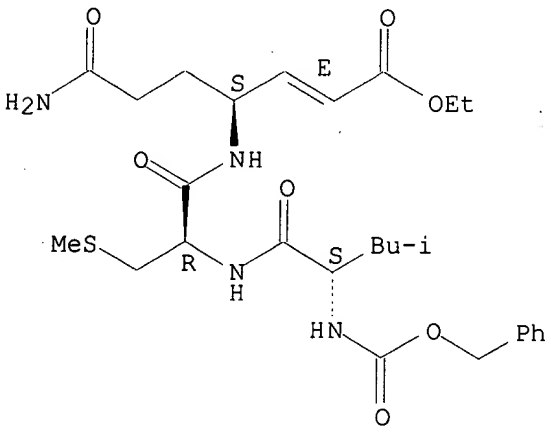
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 128:13442

L16 ANSWER 63 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **199004-99-4** REGISTRY
CN L-Cysteinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S,2E)-1-(3-amino-3-oxopropyl)-4-ethoxy-4-oxo-2-butenyl]-S-methyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H40 N4 O7 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



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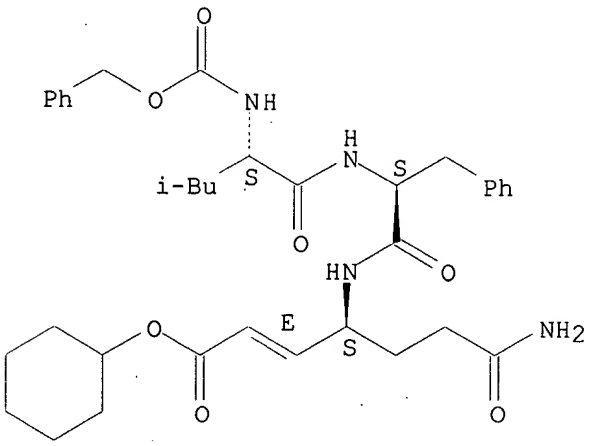
REFERENCE 1: 129:156470

REFERENCE 2: 128:13442

L16 ANSWER 111 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **199003-95-7** REGISTRY
CN L-Phenylalaninamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S,2E)-1-(3-amino-3-oxopropyl)-4-(cyclohexyloxy)-4-oxo-2-butenyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H48 N4 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



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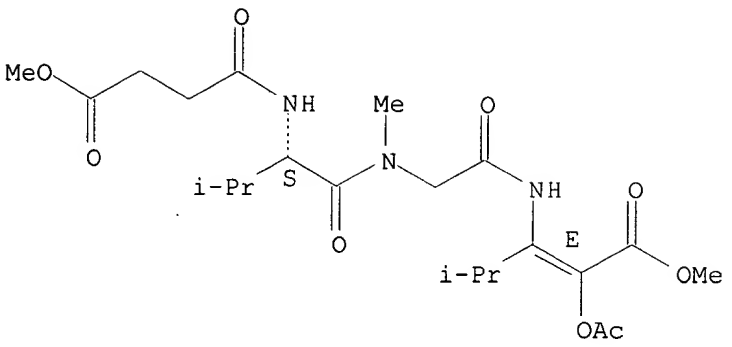
REFERENCE 1: 129:189656

REFERENCE 2: 128:13442

L16 ANSWER 128 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **192193-34-3** REGISTRY
CN Glycinamide, N-(4-methoxy-1,4-dioxobutyl)-L-valyl-N-[(1E)-2-(acetyloxy)-3-methoxy-1-(1-methylethyl)-3-oxo-1-propenyl]-N2-methyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H35 N3 O9
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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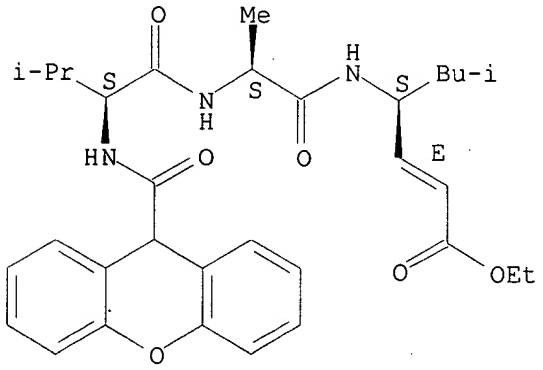
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 131:170645

REFERENCE 2: 127:95620

L16 ANSWER 130 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **187991-72-6** REGISTRY
CN L-Alaninamide, N-(9H-xanthen-9-ylcarbonyl)-L-valyl-N-[(1S,2E)-4-ethoxy-1-(2-methylpropyl)-4-oxo-2-butenyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H41 N3 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



page 8

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 126:212446

L16 ANSWER 142 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **175168-04-4** REGISTRY
CN Glycinamide, L-leucyl-L-lysyl-2,3-didehydro-.alpha.-aspartyl-L-

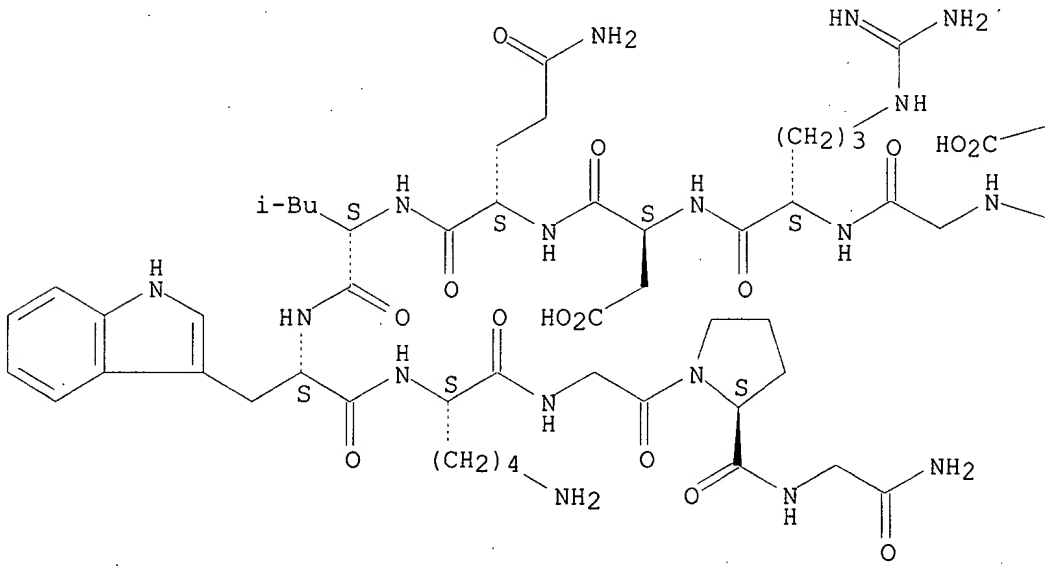
phenylalanyl-L-arginyl-L-valyl-L-tyrosyl-L-phenylalanyl-L-arginyl-L-.alpha.-glutamylglycyl-L-arginyl-L-.alpha.-aspartyl-L-glutaminyl-L-leucyl-L-tryptophyl-L-lysylglycyl-L-prolyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH
MF C114 H170 N34 O28
SR CA
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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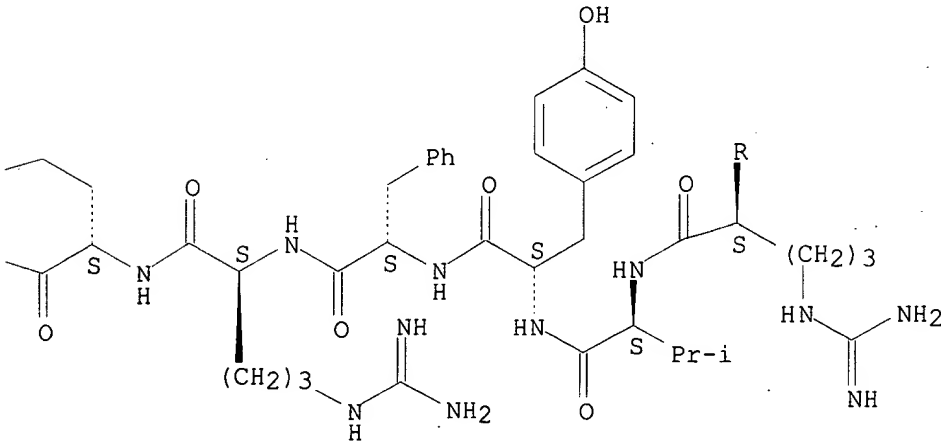

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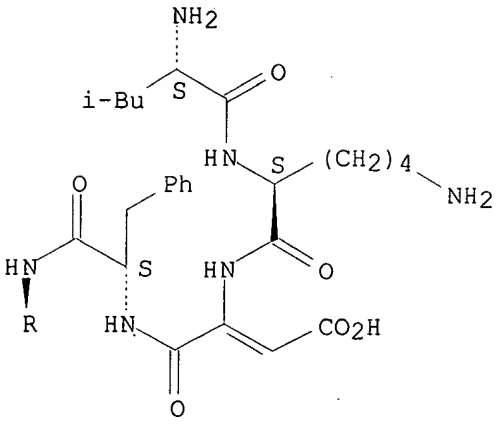

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1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

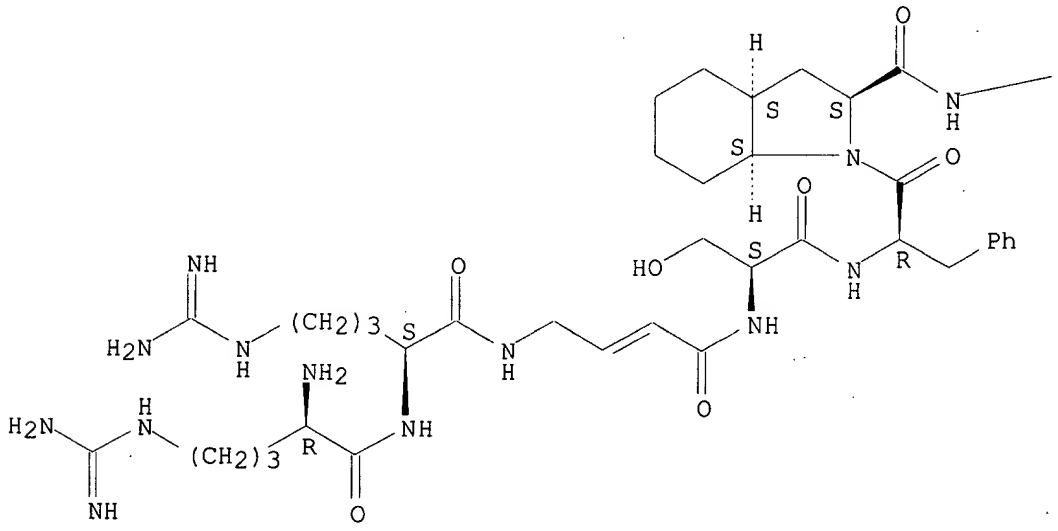
REFERENCE 1: 124:249227

L16 ANSWER 143 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **171662-73-0** REGISTRY
CN L-Arginine, N-[4-[(N2-D-arginyl-L-arginyl)amino]-1-oxo-2-butenyl]-L-seryl-D-phenylalanyl-L-(2.alpha.,3a.beta.,7a.beta.)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C43 H70 N16 O9
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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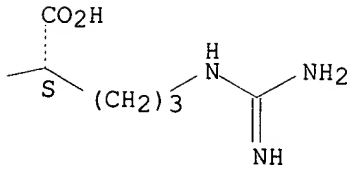

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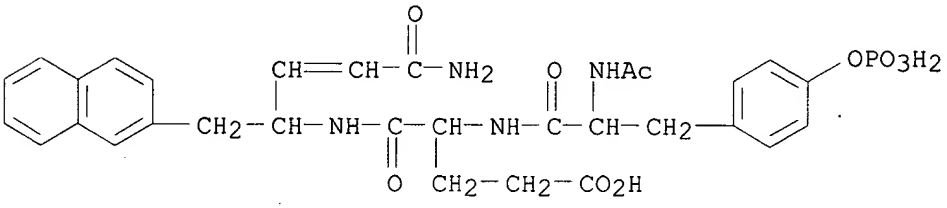
REFERENCE 1: 124:56728

L16 ANSWER 146 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **171357-91-8** REGISTRY
CN L-.alpha.-Glutamine, N2-(N-acetyl-O-phosphono-L-tyrosyl)-N-[4-amino-1-(2-naphthalenylmethyl)-4-oxo-2-butenyl]-, [R-(E)]- (9CI) (CA INDEX NAME)
MF C31 H35 N4 O10 P
SR CA
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

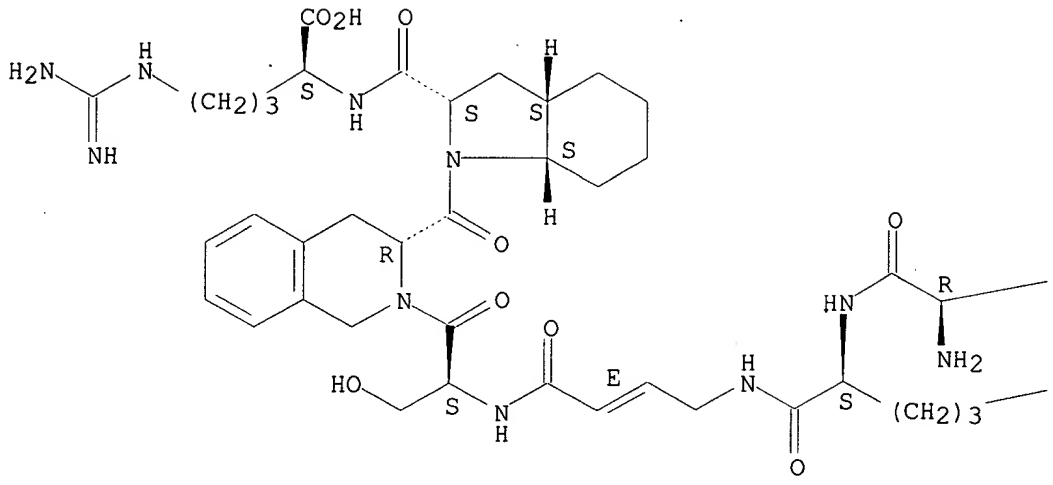
REFERENCE 1: 124:9413

L16 ANSWER 147 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **168824-56-4** REGISTRY
CN L-Arginine, D-arginyl-L-arginyl-(2E)-4-amino-2-butenoyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Arginine, N-[4-[(N2-D-arginyl-L-arginyl)amino]-1-oxo-2-butenyl]-L-seryl-D-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-(2.alpha.,3a.beta.,7a.beta.)-octahydro-1H-indole-2-carbonyl-, (E)-
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C44 H70 N16 O9
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

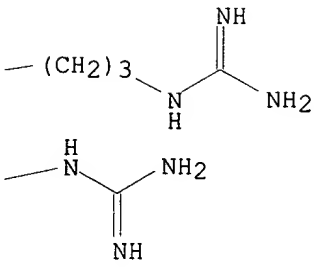
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



4 REFERENCES IN FILE CA (1957 TO DATE)
4 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 129:290436

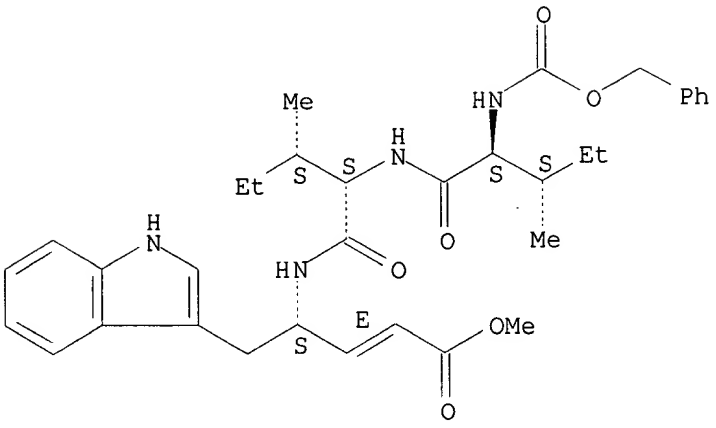
REFERENCE 2: 125:196389

REFERENCE 3: 124:56728

REFERENCE 4: 123:257408

L16 ANSWER 148 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **164785-49-3** REGISTRY
CN L-Isoleucinamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-N-[1-(1H-indol-3-ylmethyl)-4-methoxy-4-oxo-2-butenyl]-, [S-(E)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H44 N4 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

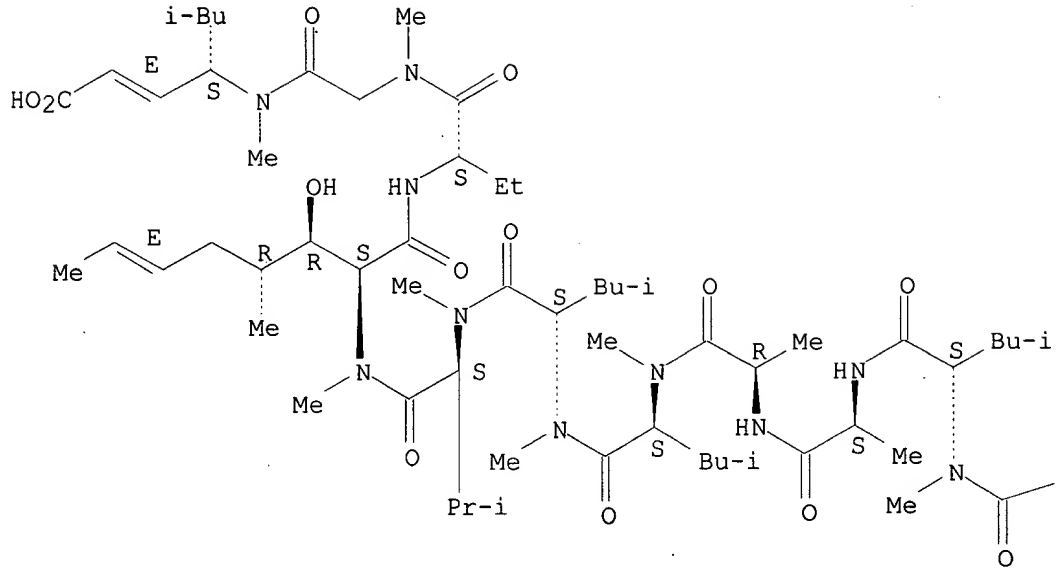
REFERENCE 1: 123:84007

L16 ANSWER 149 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **159392-12-8** REGISTRY
CN Glycinamide, L-valyl-N-methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl-(3R,4R,6E)-6,7-didehydro-3-hydroxy-N,4-dimethyl-L-2-aminooctanoyl-L-2-aminobutanoyl-N-[1-(2-carboxyethenyl)-3-methylbutyl]-N,N2-dimethyl-, [S-(E)]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C64 H115 N11 O13
SR CA
LC STN Files: CA, CAPLUS

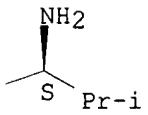
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

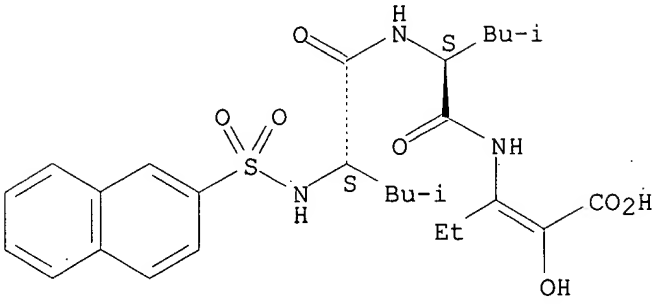


1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 122:10659

L16 ANSWER 155 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **153370-32-2** REGISTRY
CN L-Leucinamide, N-(2-naphthalenylsulfonyl)-L-leucyl-N-[1-(carboxyhydroxymethylene)propyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H37 N3 O7 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
Double bond geometry unknown.

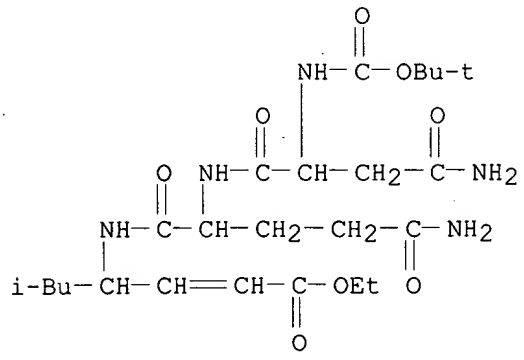


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 120:153723

L16 ANSWER 158 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **152378-15-9** REGISTRY
CN L-Glutamamide, N2-[(1,1-dimethylethoxy)carbonyl]-L-asparaginyl-N1-[4-ethoxy-1-(2-methylpropyl)-4-oxo-2-butenyl]-, [S-(E)]- (9CI) (CA INDEX NAME)
MF C24 H41 N5 O8
SR CA
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

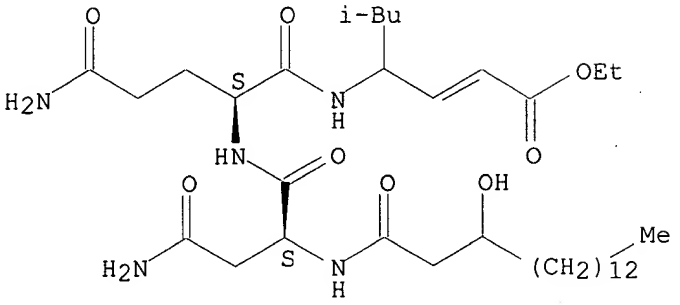
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 120:77643

L16 ANSWER 159 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **152338-63-1** REGISTRY
CN L-Glutamamide, N2-(3-hydroxy-1-oxohexadecyl)-L-asparaginyl-N1-[4-ethoxy-1-(2-methylpropyl)-4-oxo-2-butenyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH

MF C35 H63 N5 O8
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry unknown.

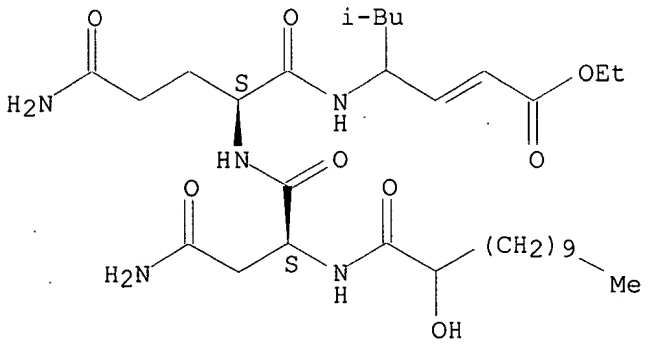


1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 120:77643

L16 ANSWER 161 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **146508-96-5** REGISTRY
CN L-Glutamamide, N2-(2-hydroxy-1-oxododecyl)-L-asparaginyl-N1-[4-ethoxy-1-(2-methylpropyl)-4-oxo-2-butenyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H55 N5 O8
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry unknown.



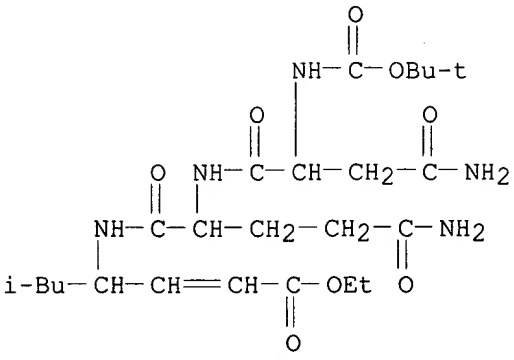
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 118:148069

L16 ANSWER 165 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **146026-89-3** REGISTRY
CN L-Glutamamide, N2-[(1,1-dimethylethoxy)carbonyl]-L-asparaginyl-N1-[4-ethoxy-1-(2-methylpropyl)-4-oxo-2-butenyl]-, (S)- (9CI) (CA INDEX NAME)

MF C24 H41 N5 O8
SR CA
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1957 TO DATE)
3 REFERENCES IN FILE CAPLUS (1957 TO DATE)

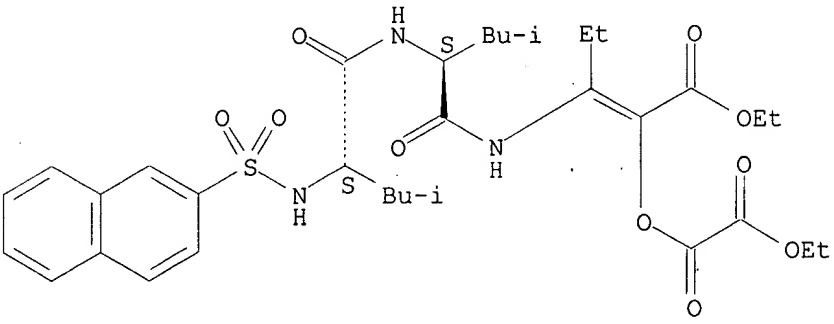
REFERENCE 1: 118:148070

REFERENCE 2: 118:148069

REFERENCE 3: 118:102476

L16 ANSWER 166 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **145731-21-1** REGISTRY
CN L-Leucinamide, N-(2-naphthalenylsulfonyl)-L-leucyl-N-[3-ethoxy-2-[(ethoxyoxoacetyl)oxy]-1-ethyl-3-oxo-1-propenyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H45 N3 O10 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry unknown.

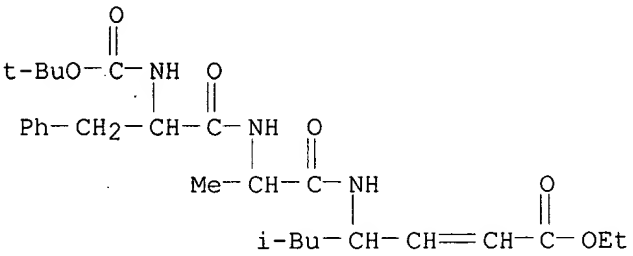


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 118:81438

L16 ANSWER 169 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **144408-31-1** REGISTRY
CN L-Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-D-phenylalanyl-N-[4-ethoxy-1-(2-methylpropyl)-4-oxo-2-butenyl]-, (S)- (9CI) (CA INDEX NAME)
MF C27 H41 N3 O6
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

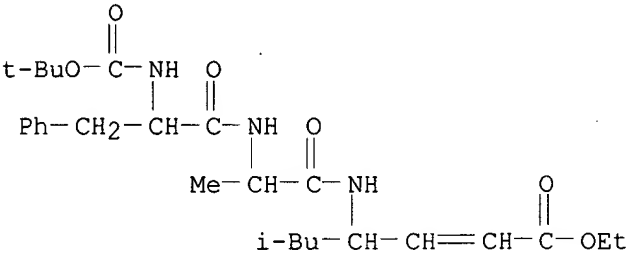


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 118:125001

L16 ANSWER 170 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **144345-56-2** REGISTRY
CN L-Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[4-ethoxy-1-(2-methylpropyl)-4-oxo-2-butenyl]-, (S)- (9CI) (CA INDEX NAME)
MF C27 H41 N3 O6
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)



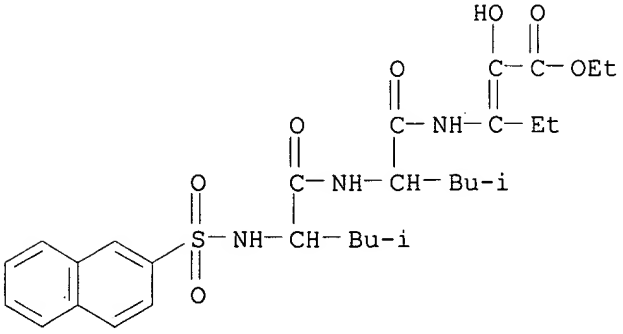
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 118:125001

L16 ANSWER 171 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **144231-97-0** REGISTRY
CN L-Leucinamide, N-(2-naphthalenylsulfonyl)-L-leucyl-N-(3-ethoxy-1-ethyl-2-

hydroxy-3-oxo-1-propenyl)- (9CI) (CA INDEX NAME)
MF C29 H41 N3 O7 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

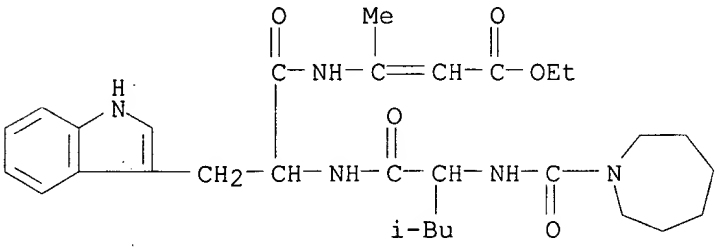


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 118:822

L16 ANSWER 174 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **141661-07-6** REGISTRY
CN D-Tryptophanamide, N-[(hexahydro-1H-azepin-1-yl)carbonyl]-L-leucyl-N-(3-ethoxy-1-methyl-3-oxo-1-propenyl)-, (E)- (9CI) (CA INDEX NAME)
MF C30 H43 N5 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

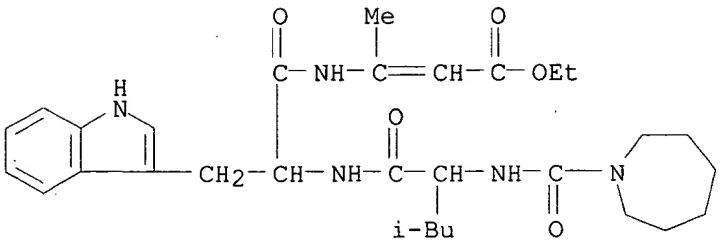


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 116:256053

L16 ANSWER 175 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **141595-35-9** REGISTRY
CN D-Tryptophanamide, N-[(hexahydro-1H-azepin-1-yl)carbonyl]-L-leucyl-N-(3-ethoxy-1-methyl-3-oxo-1-propenyl)-, (Z)- (9CI) (CA INDEX NAME)
MF C30 H43 N5 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

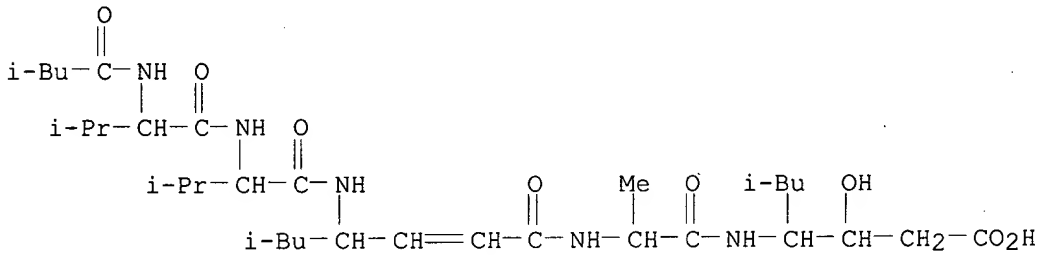


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 116:256053

L16 ANSWER 176 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **134486-20-7** REGISTRY
CN L-Valinamide, N-(3-methyl-1-oxobutyl)-L-valyl-N-[4-[[2-[[1-(2-carboxy-1-hydroxyethyl)-3-methylbutyl]amino]-1-methyl-2-oxoethyl]amino]-1-(2-methylpropyl)-4-oxo-2-butenyl]-, stereoisomer (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pepstatin A, 3-(2,3-didehydro-6-methyl-L-4-aminoheptanoic acid)-
FS PROTEIN SEQUENCE
MF C34 H61 N5 O8
SR CA
LC STN Files: CA, CAPLUS

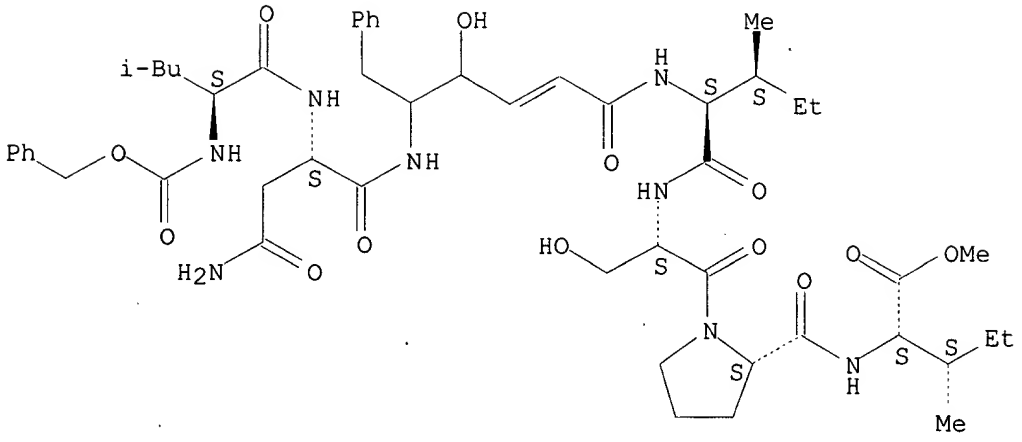


1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 115:109294

L16 ANSWER 177 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **130216-63-6** REGISTRY
CN L-Isoleucine, N-[1-[N-[N-[4-hydroxy-1-oxo-6-phenyl-5-[[N2-[N-[(phenylmethoxy)carbonyl]-L-leucyl]-L-asparaginyl]amino]-2-hexenyl]-L-isoleucyl]-L-seryl]-L-prolyl]-, methyl ester (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C51 H74 N8 O13
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry unknown.

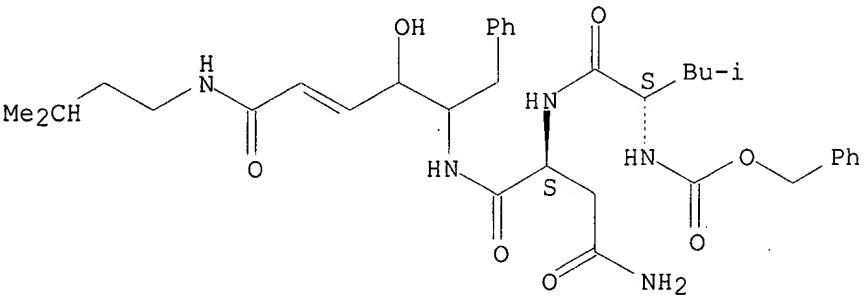


1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 114:247788

L16 ANSWER 178 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **129740-98-3** REGISTRY
CN L-Aspartamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N1-[2-hydroxy-5-[(3-methylbutyl)amino]-5-oxo-1-(phenylmethyl)-3-pentenyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H49 N5 O7
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry unknown.



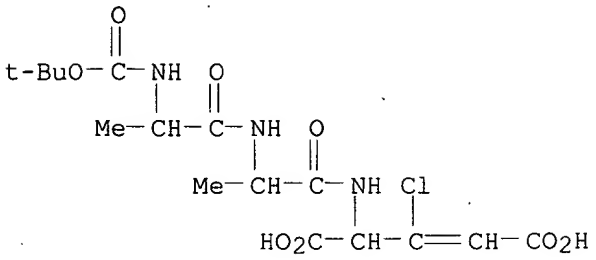
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 114:247788

L16 ANSWER 180 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **121931-73-5** REGISTRY
CN L-Glutamic acid, 3-chloro-3,4-didehydro-N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl]-L-alanyl]-, (Z)- (9CI) (CA INDEX NAME)
MF C16 H24 Cl N3 O8
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



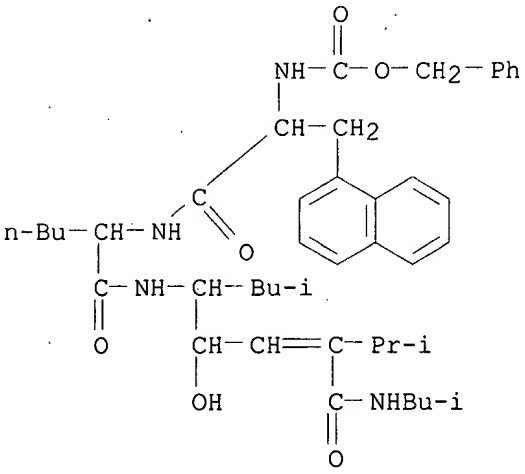
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 116:106810

REFERENCE 2: 111:78603

L16 ANSWER 182 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **118865-59-1** REGISTRY
CN L-Norleucinamide, 3-(1-naphthalenyl)-N-[(phenylmethoxy)carbonyl]-L-alanyl-N-[2-hydroxy-5-methyl-1-(2-methylpropyl)-4-[[(2-methylpropyl)amino]carbonyl]-3-hexenyl]-, [S-[R*,R*-(Z)]]- (9CI) (CA INDEX NAME)
MF C43 H60 N4 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

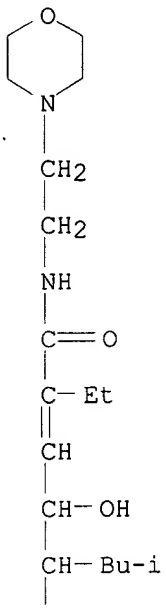
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 110:76077

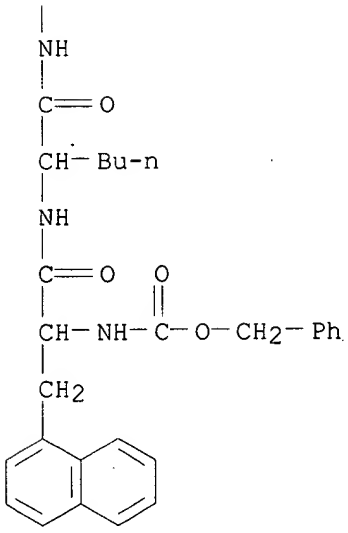
L16 ANSWER 185 OF 199 REGISTRY COPYRIGHT 2003 ACS

RN **118779-12-7** REGISTRY
CN L-Norleucinamide, 3-(1-naphthalenyl)-N-[(phenylmethoxy)carbonyl]-L-alanyl-N-[2-hydroxy-1-(2-methylpropyl)-4-[[[2-(4-morpholinyl)ethyl]amino]carbonyl]-3-hexenyl]-, [S-[R*,R*-(E)]]- (9CI) (CA INDEX NAME)
MF C44 H61 N5 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

PAGE 1-A



PAGE 2-A

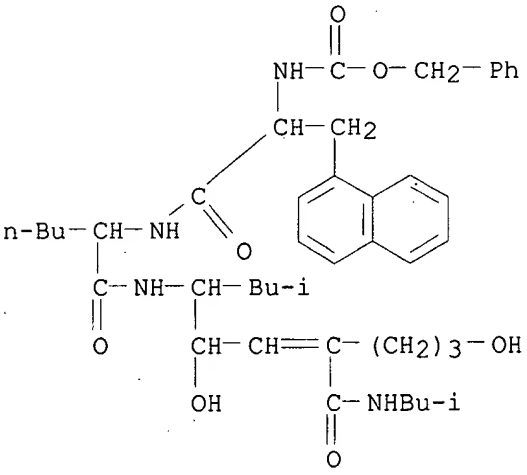


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 110:76077

L16 ANSWER 186 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **118741-45-0** REGISTRY
CN L-Norleucinamide, 3-(1-naphthalenyl)-N-[(phenylmethoxy)carbonyl]-L-alanyl-N-[2,7-dihydroxy-1-(2-methylpropyl)-4-[[(2-methylpropyl)amino]carbonyl]-3-heptenyl]-, [S-[R*,R*-(E)]]- (9CI) (CA INDEX NAME)
MF C43 H60 N4 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

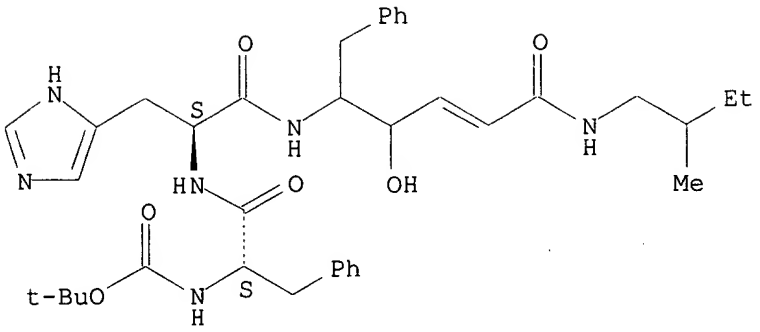


1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 110:76077

L16 ANSWER 196 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **118405-39-3** REGISTRY
CN L-Histidinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[2-hydroxy-5-[(2-methylbutyl)amino]-5-oxo-1-(phenylmethyl)-3-pentenyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H50 N6 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry unknown.



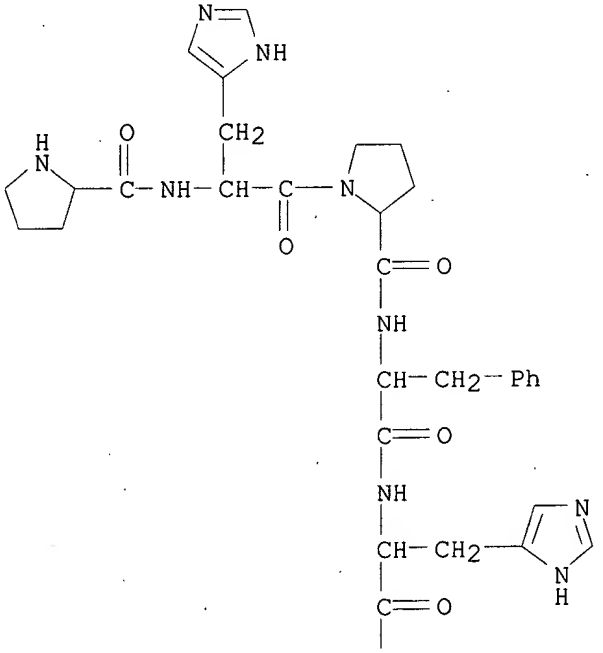
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 111:39861

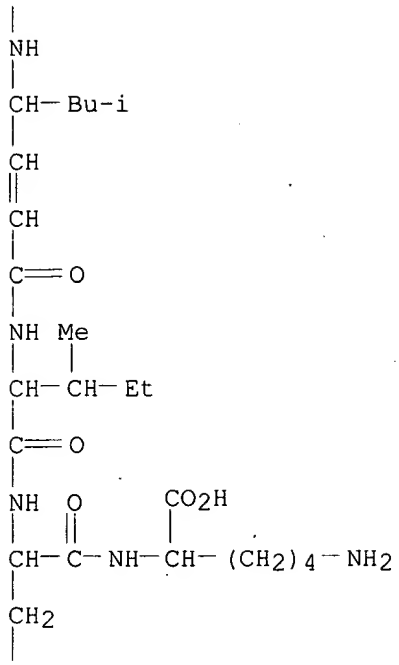
L16 ANSWER 197 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **114423-48-2** REGISTRY
CN D-Lysine, N2-[N-[N-[6-methyl-1-oxo-4-[[N-[N-[1-(N-L-prolyl-L-histidyl)-L-prolyl]-L-phenylalanyl]-L-histidyl]amino]-2-heptenyl]-L-isoleucyl]-L-histidyl]-, [S-(E)]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF C57 H82 N16 O10
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

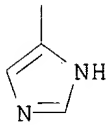
PAGE 1-A



PAGE 2-A



PAGE 3-A

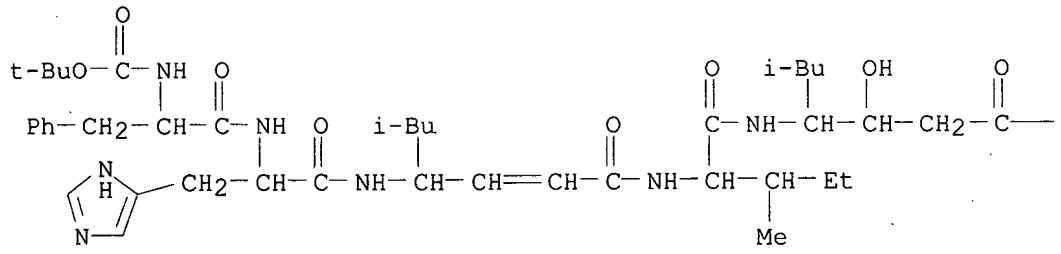


1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 109:23372

L16 ANSWER 198 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **109291-95-4** REGISTRY
CN L-Histidinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[4-[[1-[[[2-hydroxy-4-methoxy-1-(2-methylpropyl)-4-oxobutyl]amino]carbonyl]-2-methylbutyl]amino]-1-(2-methylpropyl)-4-oxo-2-butenyl]-, stereoisomer (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF C43 H67 N7 O9
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

PAGE 1-A



PAGE 1-B

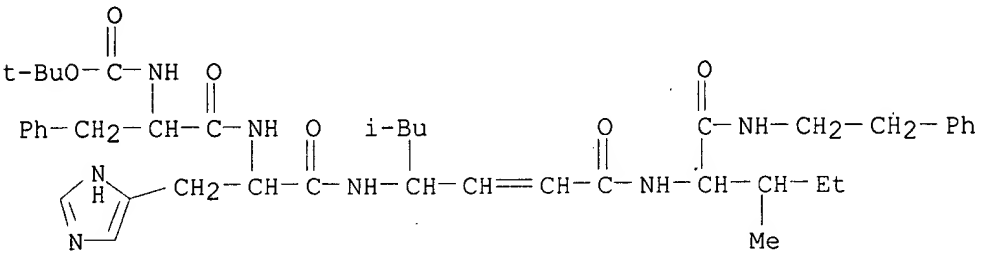
— OMe

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 107:154753

L16 ANSWER 199 OF 199 REGISTRY COPYRIGHT 2003 ACS
RN **104021-75-2** REGISTRY
CN L-Histidinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[4-[[2-methyl-1-[[(2-phenylethyl)amino]carbonyl]butyl]amino]-1-(2-methylpropyl)-4-oxo-2-butenyl]-, [1S-[1R*(R*),2R*]]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF C42 H59 N7 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK



1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 105:153553

STIC-ILL

@D1.251

From: Lukton, David
Sent: Thursday, May 29, 2003 5:52 PM
To: STIC-ILL

David Lukton
308-3213
AU 1653
Examiner room: 9B05
Mailbox room: 9B01
Serial number: 09/581511

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AU Reetz, Manfred T

Angew. Chem., Int. Ed. Engl., 1992, 31(12), 1626-9